National Advisory Committee (NAC)
for Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances
Final Meeting 7 Highlights
Interstate Commerce Commission Building
Hearing Room A
1201 Constitution Avenue, NW
Washington, D.C.
September 23-25, 1997

INTRODUCTION

The highlights of the meeting are noted below, and the meeting agenda (Attachment 1) and attendee list (Attachment 2) are attached. Highlights of the NAC Meeting 6 (June 9-11, 1997) were reviewed and approved (Appendix A).

Dr. Roger Garrett reported on the AEGL Symposium organized by Drs. Po-Yung Lu, Paul Tobin and Roger Garrett, and held at the American Chemical Society meeting in Las Vegas (September 8-11, 1997). The presentations at the symposium by NAC/AEGL participants were informative and provided a thorough overview of the AEGL process and application. Dr. Falke distributed copies of his presentation regarding his analysis of currently completed AEGL derivations.

Dr. Paul Tobin reported that Federal Register publication of proposed AEGL values for 12 chemicals was expected soon. He also indicated that an internet site is planned for presentation of the Technical Support Documents (TSDs) and relevant information. Paul also reported that Germany was amenable to recognizing AEGLs and emphasized a need for a uniform approach for deriving such values. A WWW address for AEGLs was provided: http://www.epa.gov/fedrgstr. Dr. Tobin indicated that the AEGL information would be under the heading of "Laws and Regulations."

Dr. George Rusch provided a brief overview of the 3rd Occupational Health Assoc. Workshop held in Switzerland this past summer. The considerable attendance at the workshop reflected the high level of interest in harmonization of permissible exposure values. Overall, the approaches used by different groups to derive exposure values did not vary considerably and that scholarly, complete TSDs were key requirements for meaningful and defensible, consistent values.

A question arose regarding the revision cycle for AEGLs. It was suggested that a 7-year revision cycle would probably be appropriate for AEGLs.

REPORTS FROM WORKING GROUPS AND GENERAL INTEREST ITEMS

Standing Operating Procedure (SOP) Working Group

Dr. Ernest Falke reported on the progress of the SOP Working Group and provided the NAC/AEGL with work completed thus far. It was evident that notable time and effort had been expended by the Working Group. Specific items discussed by Dr. Falke included drafts of the chemical summary sheets, guidelines for evaluating publications and data for AEGL derivations, and the organizational statement for the SOP

Working Group. Dr. Claudia Troxel will provide a pilot effort in completing the evaluation form for key and supporting studies for propylene oxide. Additional issues of concern, some of which are currently being addressed by the SOP Working Group include: cancer assessments; scientific rationale for uncertainty factor application; use of NOAEL and LOAEL values; nomenclature for AEGLs at their various developmental stages; and format/content of the AEGL TSD. Dr. Rusch commented that sharing the NAC/AEGL SOPs with other agencies and countries would be instrumental in providing credibility to the AEGLs and AEGL process.
Action Item: It was requested that NAC/AEGL members provide written comments to Dr. Falke by October 31, 1997, pertaining to SOP items that were distributed to the NAC/AEGL for comment.

AEGL PRIORITY CHEMICALS

Hydrogen Fluoride, CAS No. 7664-39-3

Chemical Manager: Mr. Larry Gephart, Exxon Biomedical Sciences
Author: Dr. Sylvia Talmage, ORNL

Larry Gephart provided an overview of hydrogen fluoride data, a chronology of the hydrogen fluoride AEGL discussions (Attachment 3), and introduced new human exposure data (Lund et al., 1997). Discussion ensued regarding revision of the 10-minute AEGL-2 value and the fact that the Dalbey (1996) data used a very sensitive model (cannulated rat) (Attachment 4). However, following in-depth discussion on revision of the 10-minute AEGL-2 value, the NAC revised the previously proposed 130 ppm value to 95 ppm as the 10-minute AEGL-2. The motion, made by Ernest Falke and seconded by Kyle Blackman, passed [YES:24, NO:0, ABSTAIN:1, ABSENT:9] (Appendix B). The 95 ppm value was based upon a NOAEL. A motion was made by Zarena Post and seconded by Nancy Kim to base AEGL-2 values on 1-hour exposure of dogs and to apply $C^2 \times t = k$ for the 30-minute, 4-hour and 8-hour time periods. Using a total uncertainty factor of 10 (3 for interspecies variability and 3 for intraspecies variability), the resulting AEGL-2 values of 95, 34, 24, 12, and 9 ppm were accepted [YES:23, NO:1, ABSTAIN:1, ABSENT:9] (Appendix C). AEGL-3 values were also revisited (Attachment 5). It was suggested that the uncertainty factor rationale be adjusted such that the interspecies variability UF =1, intraspecies variability UF = 3, and a modifying factor of 2 be applied to account for the steepness of the dose-response curve. The original AEGL-3 values of 170, 62, 44, 22, and 15 ppm were accepted by the NAC during meeting 6 of the NAC/AEGL.
Action item: Incorporate the Lund et al. data in the rationale for AEGL-1 values, noting that it was considered but that it does not impact on the status of the values.

SUMMARY OF PROPOSED AEGL VALUES FOR HYDROGEN FLUORIDE						
Classification	10-min	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1, ppm (mg/m^3)	2 (1.6)	2 (1.6)	2 (1.6)	1 (0.8)	1 (0.8)	Irritation in humans (Largent, 1960; 1961)
AEGL-2, ppm (mg/m^3)	95 (78)	34 (28)	24 (20)	12 (9.8)	9 (7.4)	NOAEL for lung irritation in cannulated rats (Dalbey, 1996)[a]; Sensory irritation in dogs (Rosenholtz et al., 1963)[b]
AEGL-3, ppm (mg/m^3)	170 (139)	62 (51)	44 (36)	22 (18)	15 (12)	Lung effects in cannulated rats (Dalbey, 1996)[c]; Lethality in mice (Wohlslagel et al., 1976)[d]

[a] 10-minute AEGL-2 value.
[b] 30-minute and 1-, 4-, and 8-hour AEGL-2 values.
[c] 10-minute AEGL-3 value.
[d] 30-minute and 1-, 4-, and 8-hour AEGL-3 values.

Dichlorodimethylsilane, CAS No. 75-78-5

Chemical Manager: Dr. Ernest Falke
Author: Dr. Cheryl Bast, ORNL

There was a brief discussion regarding the relevance of the previously accepted HCl AEGL values and their application to dichlorodimethylsilane. A motion was made (George Rodgers, seconded by William Bress) to accept the proposed new values. The motion passed [YES:21, NO:0, ABSTAIN:3, ABSENT:10] (Appendix D).

SUMMARY OF PROPOSED AEGL VALUES FOR DICHLORODIMETHYLSILANE					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1, ppm (mg/m^3)	0.45 (2.4)	0.45 (2.4)	0.45 (2.4)	0.45 (2.4)	One fourth the HCl AEGL value
AEGL-2, ppm (mg/m^3)	11 (58)	5.5 (29)	1.4 (7.4)	0.68 (3.6)	One fourth the HCl AEGL value
AEGL-3, ppm (mg/m^3)	37 (196)	26 (140)	13 (69)	9 (48)	One-half LC_{50}

Phosgene, CAS No. 75-44-5

Chemical Manager: Dr. William Bress, ASTHO
Author: Dr. Cheryl Bast, ORNL

William Bress provided a brief introduction followed by an overview of pertinent data and AEGL derivation by Cheryl Bast (Attachment 6). At the request of the Phosgene Panel of the Chemical Manufacturers Association (CMA), Dr. Werner Diller presented information based on his extensive experience with occupational exposure to phosgene (Attachment 7). Dr. Diller discussed pneumonitis and edema as critical effects and noted that pneumonitis is a clinical entity that may not be appropriate as a critical endpoint for deriving AEGL values for phosgene. Dr. Diller provided some information regarding the human experience with phosgene and expressed concerns regarding animal data and its relevance to the human experience. Dr. T.D. Landry (Dow Chemical) also presented an overview of available phosgene data (Attachment 8). Following discussion with Dr. Diller, the NAC/AEGL tabled further deliberations on phosgene pending receipt of written input from Dr. Diller with respect to data that may impact the derivation of AEGL values.

Chloroformates
Methyl chloroformate, CAS No. 79-22-1*
i-Propyl chloroformate, CAS No. 108-23-6**
Propyl chloroformate, CAS No. 109-61-5*

***Chemical Manager: Dr. Ernest Falke, U.S. EPA**
****Chemical Manager: Dr. Doan Hansen, BNL**
Author: Dr. Cheryl Bast, ORNL

Cheryl Bast provided an overview of data for the chloroformates (Attachment 9).

Propyl chloroformate

Data were unavailable for deriving AEGL values for propyl chloroformates. It was suggested that verification of the need for AEGLs for propyl chloroformate and its nomination as an AEGL chemical of concern might be appropriate. It was the consensus of the NAC/AEGL that AEGLs not be derived for propyl chloroformate until additional data and/or justification for its nomination are obtained.

i-Propyl chloroformate

Data were also insufficient for deriving AEGL values for *i*-propyl chloroformate. It was the consensus of the NAC/AEGL that no values be proposed for *i*-propyl chloroformate.

Methyl chloroformate

Following a brief overview of the derivation of the draft AEGL values for methyl chloroformate, there was some discussion regarding the use of data from a subchronic study, histopathology for extrarespiratory tissues and the over all quality of the limited data (Attachment 9). No values were proposed for AEGL-1. A motion (proposed by Loren Koller and seconded by John Hinz) to accept the proposed AEGL-2 and AEGL-3 values did not pass [YES:15, NO:8, ABSTAIN:2, ABSENT:9] (Appendix E). It was decided that a request be made to industry for additional data on this chemical.

Action item: NAC/AEGL members who voted not to accept the proposed values should send their reasons to Cheryl Bast prior to the December 1997 NAC/AEGL meeting.

Propylene Oxide, CAS No. 75-56-9

Chemical Manager: Dr. James Holler, ATSDR
Author: Dr. Claudia Troxel, ORNL

Following introductory statements by James Holler, Claudia Troxel presented a summary of relevant toxicologic data pertaining to the derivation of the draft AEGL values (Attachment 10). Susan Ripple (Dow Chemical), representing the CMA, expressed concerns of the CMA regarding the relevance of AEGL-1 and AEGL-2 endpoints and the magnitude of the uncertainty factor applied for AEGL-3 (Attachment 11). It was the consensus of the NAC/AEGL members that DNA repair was an inappropriate AEGL endpoint. Following discussions, AEGL-3 values were proposed based upon an estimated lethality threshold in mice (859 ppm for 4 hours) and a total uncertainty of 10 (3 for interspecies variability and 3 for intraspecies variability) with an n = 1.2 (based on n derived for ethylene oxide: value of 1.1 in Attachment 11 is incorrect). A motion to accept theses values was proposed by John Hinz and seconded by William Bress. The values were approved [YES:17, NO:4, ABSTAIN:2, ABSENT:11] (Appendix F). AEGL-2 values were based upon dyspnea occurring in mice exposed to 387 ppm for 4 hours (UF = 10: 3 for interspecies, 3 for intraspecies; n = 1.2). The AEGL-2 values were accepted (motion made by Mark McClanahan and seconded by Loren Koller; [YES:17, NO:0, ABSTAIN:4, ABSENT:13] (Appendix F). Vote on a motion proposed by Mark McClanahan and seconded by David Belluck that AEGL-1 values be considered not applicable passed unanimously [YES:20, NO:0, ABSTAIN:1, ABSENT:13] (Appendix F). The proposed draft values are shown in the following table.

SUMMARY OF PROPOSED AEGL VALUES FOR PROPYLENE OXIDE					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1, ppm (mg/m^3)	NA	NA	NA	NA	NA
AEGL-2, ppm (mg/m^3)	220 (520)	120 (290)	39 (86)	22 (52)	Dyspnea in mice exposed to 387 ppm for 4 hours (NTP, 1985)
AEGL-3, ppm (mg/m^3)	490 (1200)	270 (640)	86 (200)	48 (110)	Estimated threshold for lethality at 859 ppm for 4 hours (NTP, 1985)

Acrylyl Chloride, CAS No. 814-68-6

Chemical Manager: Dr. Mark McClanahan, CDC
Author: Dr. Claudia Troxel, ORNL

Drs. Troxel and McClanahan explained that data were unavailable for derivation of AEGL values for this chemical and that data for SAR approaches were also unavailable (Attachment 12). It was agreed that production volume and distribution data would be examined to determine the need to request studies on acrylyl chloride. A motion to table AEGL derivations and to address issues regarding the need to generate new data was proposed by Loren Koller and seconded by Kyle Blackman. The motion was accepted unanimously by the NAC/AEGL (Appendix G).

Boron Trichloride, CAS No. 10294-34-5

Chemical Manager: Dr. Mark McClanahan, CDC
Author: Dr. Claudia Troxel, ORNL

Dr. Claudia Troxel provided an overview of relevant data (Attachment 13). Following discussion regarding the derivation of AEGL values by analogy to hydrogen chloride or the use of boron trichloride-specific data, AEGL-3 values were based upon the Vernot et al. data: 1/3 of the 1-hour LC_{50} value of 2541 ppm in male rats was used for the derivation (847 ppm). A total UF of 30 was applied: 10 for interspecies to account for poor data base and species to species extrapolation and 3 for intraspecies. An n = 1 was used for the temporal scaling. It was noted that these values are consistent with the application of the Stokinger and Spiegl data where exposure to 50 ppm for 2 x 7 hours in rats, mice, and guinea pigs did not result in mortality when clean cages were substituted every 2 hours of the exposure (to reduce contact with the hydrolysis products formed in the cage).

This approach was considered to be consistent to that used for hydrogen chloride and was accepted by the NAC. Because HCl is a hydrolysis product of boron trichloride, the AEGL-1 and AEGL-2 values were derived by a 1/3 reduction of the accepted HCL values and would be considered as guidance values. A motion to accept AEGL-1 and AEGL-2 values was made by Robert Snyder (seconded by Nancy Kin) passed [YES:23, NO:0, ABSTAIN:0, ABSENT:11] (Appendix H). A motion to accept the AEGL-3 draft values was made by George Rodgers and seconded by Tom Sobotka. The motion passed [YES:24, NO:0, ABSTAIN:0, ABSENT:10]. The proposed draft AEGL values are shown in the following table.

SUMMARY OF PROPOSED AEGL VALUES FOR BORON TRICHLORIDE					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1, ppm (mg/m^3)	0.60 (2.9)	0.60 (2.9)	0.60 (2.9)	0.60 (2.9)	1/3 the NAC-approved HCl values: recommended as guidance levels
AEGL-2, ppm (mg/m^3)	14 (67)	7.3 (35)	1.8 (8.6)	0.90 (4.3)	1/3 the NAC-approved HCl values: recommended as guidance levels
AEGL-3, ppm (mg/m^3)	57 (270)	28 (130)	7.1 (34)	3.5 (17)	1/3 the 1-hour LC_{50} in male rats (Vernot et al., 1977)

Allyl Alcohol, CAS No. 107-18-6

Chemical Manager: Dr. Mark McClanahan, CDC
Author: Dr. Claudia Troxel, ORNL

Dr. Claudia Troxel presented an overview of the data and rationale for derivation of AEGL values (Attachment 14). During initial discussions of the data, it was stated that an individual at Rutgers was conducting research on the metabolism and toxicity of allyl alcohol and that data from such studies may be useful in assessments for this chemical. Following discussions of various approaches for setting AEGL-3 values, a set of values based upon a 1-hr LC_{50} (value adjusted for 25% loss of chemical during exposure) in

rats (UF = 10, n = 2) was unanimously accepted (motion by John Hinz, seconded by William Pepelko; [YES:21, NO:1, ABSTAIN:0, ABSENT:12] (Appendix I). It was noted that the AEGL-3 values were supported by the NOEL for death of 200 ppm for 1 hour in rats, mice, and rabbits. A motion was made by Robert Snyder and seconded by Loren Koller to accept the AEGL-2 values as originally proposed by Drs. Troxel and McClanahan. The motion was passed [YES:18, NO:4, ABSTAIN:0, ABSENT:12] (Appendix I). It was noted that the values are supported by a 60 ppm exposure for 7 hours. The AEGL-1 values as originally proposed were also accepted (motion by William Bress, seconded by Zarena Post; [YES:18, NO:4, ABSTAIN:0, ABSENT:12]) (Appendix I). The proposed draft values are summarized in the following table.

SUMMARY OF PROPOSED AEGL VALUES FOR ALLYL ALCOHOL					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1, ppm (mg/m^3)	1.8 (4.4)	1.8 (4.4)	1.8 (4.4)	1.8 (4.4)	Mean odor detection threshold (AIHA, 1989)
AEGL-2, ppm (mg/m^3)	15 (36)	11 (26)	5.3 (13)	3.7 (9.0)	Exposure to 40 ppm for 7 hr/d caused irritation during the first few exposures (Dunlap et al., 1958)
AEGL-3, ppm (mg/m^3)	35 (85)	25 (61)	13 (31)	8.8 (21)	1/3 of the 1-hour LC_{50} in rats (the 1-hour LC50 value adjusted for 25% loss of chemical during exposure) (Dunlap et al., 1958)

ADMINISTRATIVE ISSUES

Plans for future NAC/AEGL meeting dates were discussed. The following are proposed meeting dates:

NAC-8, December 8-10, 1997,Washington, DC
NAC-9, March 10-12, 1998, Oak Ridge, TN
NAC-10, June 15-17, 1998, Washington, DC
NAC-11, September 15-17, 1998, Washington, DC

Draft highlights of NAC-7 were prepared by Drs. R. A. Young and P. Y. Lu of ORNL.

LIST OF ATTACHMENTS

The attachments were distributed during the meeting and will be filed in the EPA Docket Office.

1. NAC Meeting No. 7 Agenda
2. NAC Meeting No. 7 Attendee List
3. Overview of Hydrogen fluoride - Larry Gephart
4. Data analysis of Hydrogen fluoride - Larry Gephart
5. Additional data analysis of hydrogen fluoride - Sylvia Talmage and Larry Gephart
6. Data analysis of Phosgene - Cheryl Bast
7. Data analysis of Phosgene - Werner Diller
8. Data analysis of Phosgene - T.D. Landry
9. Data analysis of Chloroformates - Cheryl Bast
10. Data analysis of Propylene oxide - Claudia Troxel
11. Additional data analysis of Propylene oxide from Courtney M. Price, CMA
12. Data analysis of Acrylyl chloride - Claudia Troxel
13. Data analysis of Boron trichloride - Claudia Troxel
14. Data analysis of Allyl alcohol - Claudia Troxel
16. Data analysis of TDI data - Carol Forsyth
17. Data analysis of derivation of AEGLs for Aniline - Sylvia Talmage
18. Introduction of isopropyl chloroformate - Doan Hansen
19. Data summaries of isopropyl chloroformate and Methyl and Propyl chloroformate - Cheryl Bast

LIST OF APPENDICES

A. Approved NAC-6 Meeting Highlights
B. Ballot for Hydrogen fluoride
C. Ballot for Hydrogen fluoride
D. Ballot for Dichlorodimethylsilane
E. Ballot for Methyl chloroformate
F. Ballot for Propylene oxide
G. Ballot for Acrylyl chloride
H. Ballot for Boron trichloride
I. Ballot for Allyl alcohol

National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances

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NAC-7

Agenda

Tuesday, Sept. 23, 1997

10:00 - 10:15	AM	Introduction and approval of NAC-6 highlights (George Rusch)
10:15 - 10:30		Program Director and Designated Federal Officer report (Roger Garrett and Paul Tobin)
10:30 - 12:00		SOP Workgroup progress report (Ernie Falke)
12:00 - 1:00	PM	**Lunch**
1:00 - 2:00		Hydrogen fluoride (Larry Gephart)
2:00 - 3:00		Phosgene (Bill Bress/Cheryl Bast)
3:00 - 3:15		**Break**
3:15 - 4:30		Phosgene (continued)
4:30 - 5:00		Carbon tetrachloride (Bill Bress/Bob Young)

Wednesday, Sept. 24, 1997

8:30 - 10:00	AM	Carbon tetrachloride (continued)
10:00 - 10:15		**Break**
10:15 - 11:30		Dichlorodimethylsilane (Ernie Falke/Cheryl Bast)
11:30 - 12:30		**Lunch**
12:30 - 1:45	PM	Propylene oxide (Jim Holler/Claudia Troxel)
1:45 - 2:45		Acrylyl chloride (Mark McClanahan/Claudia Troxel)
2:45 - 3:00		**Break**
3:00 - 5:00		Methyl-, Propyl-, *i*-Propyl chloroformates (Ernie Falke, Doan Hansen/Cheryl Bast)

Thursday, Sept. 25, 1997

8:30 - 9:30	AM	Allyl alcohol (Mark McClanahan/Claudia Troxel)
9:30 - 10:30		Boron trichloride (Mark McClanahan/Claudia Troxel)
10:30 - 10:45		**Break**
10:45 - 12:00		Brief review of literature of sulfur dioxide, sulfur trioxide, and sulfuric acid (Cheryl Bast)
12:00 - 1:00	PM	Administrative issues
1:00		Adjournment

ATTENDANCE SHEET

SUBJECT: NAC AEGL Comm.

DATE: Sept. 23, 1997

TIME:

LOCATION: ICC BUILDING ~~Ariel Rios - Green Room~~

Name	Signature	Organization	Phone Number
Lorraine Hester	Lorraine Hester	EPA	202-260-4665
Richard Wood	Richard Wood	Dir Products & Chem	610-481-5756
Walden Dalbey	Walden Dalbey	Mobil	609-224-4616
Don Veraska	Don Veraska	BNA	202-452-4584
Sally Benjamin	Sally L. Benjamin	CRI	612-721-1809
Tom Sabotka	Thomas J. Sabotka	FDA	301-594-5881
Bill Pepelko	William Pepelko	EPA	202-260-5904
John P. Hinz	J P Hinz	USAF	(210) 536-6136
Po-Yung Lu	Po-Yung Lu	ORNL	(423) 574-7803
Cheryl Bast	Cheryl Bast	ORNL	423-574-7581
Robert Young	Robert Young	ORNL	(423) 574-4573
Mark A McClanahan	Mark A McClanahan	CDC	770-488-7297
Jim Holler	Jim Holler	ATSDR	404-639-6308
Lynn Beasley	Lynn Beasley	USEPA/SUPERFUND	703-603-9086
Luz Claudio	Luz Claudio	Mount Sinai/NYC	212 241 6173
Steven Barbee	S Barbee	Olin Corp/AIHA	203-495-8550 x 5435
Larry Gephart	Larry Gephart	Exxon Biomedical	908 873-6319
Rick Niemeier	Rick Niemeier	NIOSH	(513) 533-8388
George Cushmac	George Cushmac	DOT	202-366-4493
George Alexeeff	George Alexeeff	Cal/EPA	510-540-3324
David A. Bellum	D. A. Bell	MPCA	612-296-7871
Kyle Blackman	Kyle Blackman	FEMA	202-646-4676
Paul Tobin	Paul Tobin	EPA	202 260-1736
George Rusch	George M. Rusch	Allied Signal	201-455-3672
Robert Garrett	Robert Garrett	EPA	202-260-4302

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Name	Signature	Organization	Phone Number
Robert Snyder		Rutgers Univ	908-445-3720
Richard Thomas		JCEH	703-734-1454
Nancy Kim		NYS DOH	518-458-6435
Bob Benson		EPA-Region 8	303-312-7070
Bill Bress		ASTHO	802-863-7598
Zarena Post		TNRCC	512-239-1332
Loren Koller		OSU	541-737-5347
Tom Hornshaw		IL EPA	217-785-0830
Georgi Rodgers		AARC	502-852-8626
Kenneth R. Still		USNAVY	937-255-6058 x202
Joseph F. King		US Army Env. Ctr	(410) 671-1535
Morris J Warren		ABERCO Inc	301-469-7090
Jon C Shepherd		CMA Phos. Power	(281)471-5147 x245
Tim Landry		CMA " "	517 636 2733
Welsor D. Diller		CMA	Gurney 214/47381
Chris Trent		CMA	703 741-5627

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Walden Dalbey	Walden Dalbey	Mobil	609-224-4616
Don Vrooska	Don Vrooska	BNA	202-452-4584
Sally Benjamin	Sally L. Benjamin	CRI	612-724-809
Tom Sobotka	Thomas J. Sobotka	FDA	301-594-5881
Bill Pepelko	William Pepelko	EPA	202-260-5904
John P. Hinz	JP Hinz	USAF	(210) 536-6136
Po-Yung Lu	Po-Yung Lu	ORNL	(423) 574-7803
Cheryl Bast	Cheryl Bast	ORNL	423-574-7581
Robert Young	Robert Young	ORNL	(423) 574-4573
Mark A McClanahan	Mark A McClanahan	CDC	770-488-7297
Jim Holler	Jim Holler	ATSDR	404-639-6308
Lynn Beasley	Lynn Beasley	USEPA/Superfund	703-603-9086
Luz Claudio	Luz Claudio	Mount Sinai/NYC	212 241 6173
Steven Barbee	Steven Barbee	Olin Corp/AIHA	203-495-8550 x 5435
Larry Gephart	Larry Gephart	Exxon Biomedical	908 873-6319
Rick Niemeier	Rick Niemeier	NIOSH	(513) 533-8388
George Cushmac	George Cushmac	DOT	202-366-4493
George Alexeeff	George Alexeeff	Cal/EPA	510-540-3324
David A. Bellum	David A. Bellum	MPCA	612-296-7871
Kyle Blackman	Kyle Blackman	FEMA	202-646-4676
Paul Tobin	Paul Tobin	EPA	202 260-1736
George Rusch	George Rusch	Allied Signal	201-455-3672
Robert Garrett	Robert Garrett	EPA	202-260-4302

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Wesley D. Diller		CMA	Gurney 214/47381
Chris Trent		CMA	703 741-5627

3

Attachment II

HF AEGLS

L. A. Gephart

HUMAN DATA

- LETHAL EFFECTS
  - No actual data due to ethical considerations
- "SERIOUS EFFECTS" (TABLE 2)
  - 3 Older studies, with limitations
    - Exposure levels were either low and repeated or higher but brief
    - Effects were less serious than indicated by definition of AEGL-2
    - Small number of people used and all are assumed to be healthy adults
    - Differences in HF collection and analysis methods
  - 3 Accident exposure reconstruction studies, with limitations
    - Uncertainty in exposure estimates
    - Lack of controls
    - Problems with symptom survey / reporting
- MINIMAL / NO EFFECTS
  - 2 Studies in workers exposed repeatedly to HF, fluoride
    - No respiratory effects observed at moderate exposure levels
    - Combined exposure to HF / fluorides limits usefulness

HF

- COLORLESS, FUMING GAS (OR LIQUID) WITH HIGH WATER SOLUBILITY
- USES: FLUORINATING AGENT IN ORGANIC AND INORGANIC REACTIONS, CATALYST IN ALKYLATION AND POLYMERIZATION REACTIONS, PRODUCTION OF FLUORINE AND ALUMINUM FLUORIDE, ADDITIVE IN LIQUID ROCKET PROPELLANTS, GLASS ETCHING
- PRIMARY TOXICITY CONCERN FOR ACUTE INHALATION EXPOSURE: SEVERE IRRITATION
  - Lower concentrations scrubbed in nasal passages, upper respiratory tract
  - Higher concentrations reach deep lung producing necrosis, pulmonary edema
- TOXICITY CONCERNS FOR REPEATED EXPOSURES: RENAL EFFECTS, OSTEOFLUOROSIS
- DATA FROM SIMULATED ACCIDENTAL CATASTROPHIC RELEASES FROM COMPRESSED GAS CYLINDERS INDICATE CRITICAL EXPOSURE DURATIONS ARE IN THE RANGE OF 2-10 MINUTES

TABLE 2
SUMMARY OF IRRITANT EFFECTS IN HUMANS

CONCENTRATION (ppm)	EXPOSURE TIME	EFFECTS	REFERENCE
0.2 - 0.7	1 Hour	no to low sensory and lower airway irritation; no change in FEV_1, decrease in FVC	Lund et. al., 1997
0.85 - 2.9	1 Hour	no to low sensory and lower airway irritation; no change in FVC, FEV_1	Lund et. al., 1997
3.0 - 6.3	1 Hour	no eye irritation, upper (3/14 subjects) and lower (1/14 subjects) airway irritation;[a] no change in FVC, FEV_1	Lund et. al., 1997

[a] Upper airways: symptoms of eye, nose, and throat irritation; lower airways: symptoms of chest tightness, coughing, expectoration, wheezing.
FVC = forced vital capacity.
FEV_1 = forced expiratory volume in one second.

TABLE 2
SUMMARY OF IRRITANT EFFECTS IN HUMANS

Concentration (PPM)	Exposure Time	Effects	Reference
1.42	6 Hours / day, 15 days	No noticeable effect (single subject)	Largent 1960, 1961
2.59-4.74 (avg.) 0.9-8.1 (range)	6 Hours / day, 10-50 days	Slight irritation of the skin, nose, and eyes; sour taste in mouth	Largent 1960, 1961
~5.76 (avg.) 4.2-9.1 (range)	6 Hours	Irritant effect followed by accommodation	Collings et al. 1951
32	3 Minutes	"tolerated" with discomfort' mild irritation of eyes and nose	Machle et al. 1934
61	~1 Minute	Eye and nasal irritation	Machle et al. 1934
122	~1 Minute	Marked eye and respiratory irritation, skin irritation, highest concentration tolerated for > 1 minute	Machle et al. 1934

[a]Exposure to gaseous HF and silicon tetrafluoride.

TABLE 4
SUMMARY OF ACUTE LETHAL INHALATION DATA IN LABORATORY ANIMALS

Species	Concentration (ppm)	Exposure Time	Effect[a]	Reference
Rat	4,970	5 Minutes	LC_{50}	Rosenholtz et al. 1963
Rat	14,640[b] 10,700[b]	5 Minutes	LC_{50}	Haskell Laboratory 1988a, 1988b
Rat	12,440	5 Minutes	LC_{10}	Higgins et al. 1972
Rat	18,200	5 Minutes	LC_{50}	Higgins et al. 1972
Rat	25,690	5 Minutes	LC_{100}	Higgins et al. 1972
Rat	2,689	15 Minutes	LC_{50}	Rosenholtz et al. 1963
Rat	6,620[b] 1,020[c]	15 Minutes	LC_{50}	Haskell Laboratory 1988a, 1988b
Rat	2,042	30 Minutes	LC_{50}	Rosenholtz et al. 1963
Rat	2,890[b] 1,020[c]	30 Minutes	LC_{50}	Haskell Laboratory 1988a, 1988b
Rat	1,307	60 Minutes	LC_{50}	Rosenholtz et al. 1963
Rat	1,108	60 Minutes	20% Mortality	Wohlslagel et al. 1976
Rat	1,395	60 Minutes	LC_{50}	Wohlslagel et al. 1976
Rat	2,300	60 Minutes	LC_{50}	Haskell Laboratory 1990
Rat	1,630[b] 540[c]	60 Minutes	LC_{50}	Haskell Laboratory 1988a, 1988b
Rat	190	6 Hours	LC_{100}	Morris and Smith 1982
Mouse	6,247	5 Minutes	LC_{50}	Higgins et al. 1972
Mouse	11,010	5 Minutes	LC_{100}	Higgins et al. 1972
Mouse	342	60 Minutes	LC_{50}	Wohlslagel et al. 1976
Guinea Pig	>1,220-1,830	5 Minutes	Death in a Significant Number of Animals	Machle et al. 1934
Guinea Pig	4,327	15 Minutes	LC_{50}	Rosenholtz et al. 1963
Rabbit	>1,220-1,830	5 Minutes	Death in a Significant Number of Animals	Machle et al. 1934

a LC_{50} and LC_{100} values were obtained at 3 hours post exposure (Morris and Smith 1982), 7 days post exposure (Higgins et al. 1972); 14 days post exposure (Rosenholtz et al. 1963, Wohlslagel et al. 1976, Haskell Laboratory 1988a, b).
b Tested at relative humidity of <10%.
c Tested at relative humidity of 40-50%.

ANIMAL DATA

- ACUTE LETHALITY DATA (TABLE 4)
  - Good data base for exposure durations of 5-60 minutes
  - Limited data for 4-8 hours
  - Differences in results partially due to differences in analytical methods
  - Lethality data tend to follow $C^2 \times T = K$ (Alexeeff, Ten Berg)
- ACUTE SERIOUS EFFECTS DATA (TABLE 3)
  - Limited data, mostly from clinical observations in LC_{50} studies*
    - Exception: Study by Stavert

* Excluding data from the PERF HF toxicity studies

SUMMARY OF SAMPLING / ANALYTICAL METHODS IN HF STUDIES

Study	Sampling and Analysis Method
Haskell Lab 1988, 1989	Collection into 0.1 n NaOH using glass impingers, diluted 1:1 with total ionic strength adjusting buffer (TISAB). Analysis using fluoride specific ion electrode
Haskell Lab, 1990	As above except impinger inlets and outlets were coated with teflon
Higgins et al., 1972	Collection into "aqueous reagent solutions" and measurement via specific ion electrode
Largent, 1960, 1961	Unknown
Machle et al., 1934	Collection into NaOH using a glass apparatus. Analysis using titration with Nitric acid and phenol red
Machle and Evans, 1940	Unknown but likely as above
Morris and Smith, 1990	Similar to Haskell 1988-9 except collection was directly into TISAB.
Rosenholtz et al., 1963	Collection into gas bottles, or, 0.2 N NaOH solutions. Analyses via the "volumetric method"
Stavert et al., 1991	As per Haskell Lab, 1988-1989
Wohlslagel et al, 1976	Collection into "gas scrubber column with known amounts of aqueous reagent absorber." Analysis using specific ion electrodes

HF SAMPLING / ANALYTICAL CONSIDERATIONS

- BEST METHOD (DUPONT, 1990):
  - Use glass impingers fitted with teflon inlet / outlet
  - Sample at air flow rate of 1.2 - 1.6 L / minute
  - Collect into 0.1 N NaOH
  - Dilute 1:1 with buffer
  - Analyze with fluoride specific ion electrode
- OLDER METHODS
  - Use of all glass impingers: HF levels 25% lower than actual
  - Use of low air flow rates: HF levels 12% lower than actual

PROPOSED 10-MINUTE AEGL-2 FOR HF
AEGL COMMITTEE MEETING

December 16, 1996

L. A. Gephart

96MR 1047

UNCERTAINTY FACTOR CONSIDERATIONS (cont'd)

- IS THE ENDPOINT ACCURATELY DEFINED BY OUR DEFINITION OR IS IT A MORE OR LESS SERIOUS EFFECT?
  - The endpoint used meets our definition i.e. a NOAEL from a study designed to assess AEGL 2 effects - the endpoints evaluated included extensive lung histology, pulmonary function, etc.
- WAS THE STUDY ON WHICH THE AEGLs WERE BASED WELL-DESIGNED, CONDUCTED AND REPORTED?
  - Yes, the study was designed to establish short-term AEGLs and we have the full report
- DO WE NEED TO EXTRAPOLATE THE EXPOSURE DURATION?
  - No, the study exposure duration = AEGL time frame

UNCERTAINTY FACTOR CONSIDERATIONS

- ARE WE USING A THRESHOLD, OR A NOAEL?
  - We are using a NOAEL (950 ppm)
- DO WE HAVE INFORMATION ON A SINGLE SPECIES OR FOR MULTIPLE SPECIES?
  - We have data for multiple species
- ARE THE DATA CONSISTENT ACROSS SPECIES?
  - When differences due to exposure measurement are accounted for, the data are fairly consistent across species
- DO WE EXPECT MAN TO BE UNIQUELY MORE OR LESS SENSITIVE THAN THE TEST SPECIES?
  - No - Lab animals and humans respond similarly to respiratory irritants; cannulation used to simulate human mouth breathing

RESULTS

- SERIOUS EFFECTS OBSERVED AT 1764 PPM
  - Histopathological effects in the lung
  - Pronounced function/biochemical alterations
- MARGINAL EFFECTS AT 950 PPM
  - No histopathological changes in the lungs or bronchi
  - Histological changes in trachea similar to control
  - Functional/biochemical changes minimal
- THRESHOLD FOR SERIOUS EFFECTS AT ~ 1300 PPM

SELECTION OF KEY STUDY

- RECOMMEND STUDY IN RATS REPORTED BY DALBY (1996)
  - Designed to evaluate AEGL-2 effects
  - Included 10-minute exposures
  - Employed sensitive model (cannulated rat)
  - Included multiple, sensitive biological endpoints
    - + Pulmonary function
    - + Bronchoalveolar lavage
    - + Hematology and serum chemistry
    - + Histopathology
    - + Nasal resistance (nose breathing groups)

CONCLUSIONS

- CONDITIONS SUPPORT USE OF LOWER UNCERTAINTY FACTOR
  - Used NOAEL rather than a threshold
  - Have data for multiple species and results are consistent
  - Endpoint of concern has lower response variability
  - Used data from cannulated animal
  - Used data from a study that was well-designed and reported
  - Did not need to extrapolate
- UNCERTAINTY FACTOR RECOMMENDATION
  - 3X intra-species UF
  - 3X intra-species UF
  - 10X total UF
- 10-MINUTE AEGL-2 RECOMMENDATION
  - 130 ppm (if based on "threshold" for serious effects
  - 95 ppm (if based on NOAEL)

Revision of Proposed Hydrogen Fluoride AEGLs

June 1997

ORNL Staff Scientist:
Sylvia S. Talmage

Chemical Manager:
Larry Gephart

Attachment 5

INCONSISTENCIES IN THE USE OF UNCERTAINTY FACTORS

Inconsistency: Used interspecies uncertainty factor of 10 (rat was not the most sensitive species) and intraspecies uncertainty factor of 3 for 30-minute and 1-hour AEGL-2. However, hydrogen fluoride was delivered directly to the trachea (a conservative model that mimics human mouth breathing), thus bypassing the scrubbing action of the nasal passages. In addition, the endpoint was a no-effect concentration (950 ppm for 10 minutes). Interspecies and intraspecies uncertainty factors of 3 and 3 are generally used for irritant gases.

Change: Use total uncertainty factor of 10 (3 and 3). Results are 30-minute and 1-hour AEGL-2 values of 55 and 39 ppm instead of 18 and 13 ppm.

HYDROGEN FLUORIDE

INCONSISTENCIES IN THE USE OF DATA

Inconsistency: For derivation of the 10-minute AEGL-2, the mean of a no-effect (950 ppm) and a lethal concentration (1/20 deaths at 1764 ppm) of orally-cannulated rats was used (1300 ppm), whereas the no-effect 950 ppm concentration was used to derive the 30-minute and 1-hour AEGL-2 values.

Change: Use the 10-minute 950 ppm no-effect concentration to derive the 10-minute AEGL-2. Result is 95 ppm instead of 130 ppm.

The combined interspecies and intraspecies uncertainty factor of 10 (3 and 3) remains the same.

INCONSISTENCIES IN THE USE OF UNCERTAINTY FACTORS (con't)

Inconsistency: Used interspecies uncertainty factor of 2 for the 30-minute and 1-, 2-, 4-, and 8-hour AEGL-3 values (based on the LC_0 of 263 ppm for the mouse, the most sensitive species).

Change: Use interspecies uncertainty factor of 1 because mouse is 2-4 times more sensitive than rat; if we use UF of 2 or 3, the AEGL-3 values will be below the AEGL-2 values. Use 1-hour mouse LC_{01} (200 ppm) instead of mouse LC_0 (263 ppm). Results are 30-minute and 1-, 4-, and 8-hour AEGL-3 values of 94, 67, 33, and 24 ppm.

HYDROGEN FLUORIDE

ADJUSTMENT OF ENDPOINT

Inconsistency: For AEGL-3, used LC_0 for mouse (263 ppm for 1 hour) when data allowed calculation of an LC_{01}, the accepted threshold for lethality.

Change: Use LC_{01} (200 ppm) instead of LC_0 (263 ppm).

SUMMARY OF ORIGINAL PROPOSED AEGL VALUES					
Classification	Exposure Duration				
	10-Minute	30-Minute	1-Hour	4-Hour	8-Hour
AEGL-1 (Nondisabling)	2 ppm (1.6 mg/m^3)	2 ppm (1.6 mg/m^3)	2 ppm (1.6 mg/m^3)	1 ppm (0.8 mg/m^3)	1 ppm (0.8 mg/m^3)
AEGL-2 (Disabling)	130 ppm (107 mg/m^3)	18 ppm (15 mg/m^3)	13 ppm (11 mg/m^3)	10 ppm (8 mg/m^3)	7 ppm (6 mg/m^3)
AEGL-3 (Lethal)	170 ppm (139 mg/m^3)	62 ppm (51 mg/m^3)	44 ppm (36 mg/m^3)	22 ppm (18 mg/m^3)	15 ppm (13 mg/m^3)

HYDROGEN FLUORIDE

BACKUP STUDIES TO THE AEGL-2 AND AEGL-3 VALUES

AEGL-2

Mouse RD_{50} = 151 ppm (0.1 x RD_{50} = 15 ppm)

0.1 x RD_{50} can be tolerated for hours with some irritation (Alarie)

AEGL-3

All of the animal data support the new AEGL-3 values:

Nose-breathing animals

monkey, 1-hour LC_0 of 690 ppm/10 = 69 ppm (MacEwen and Vernot, 1970)
rat, 1 hour no lung lesions of 1630 ppm/10 = 163 ppm (Haskell, 1989)
rat, 1 hour respiratory distress of 1224 ppm/10 = 122 ppm (Dalbey, 1996)
rat, 1 hour LC_0 of 1087 ppm/10 = 109 ppm (Wohlslagel et al. 1976)
guinea pig, 30 minutes no deaths, 1377/10 = 138 ppm (Rosenholtz et al., 1963)
guinea pig, 30 minutes no deaths, 1220/10 = 122 ppm (Machle et al., 1934)
rabbit, 30 minutes no deaths 1220/10 = 122 ppm (Machle et al., 1934)

Orally-cannulated rats:

1700 ppm for 10-minutes = 1/20 deaths
1700/10, scaled, = 1-hour value of 69 ppm

HYDROGEN FLUORIDE

SUMMARY OF REVISED PROPOSED AEGL VALUES					
Classification	**Exposure Duration**				
	10-Minute	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1 (Nondisabling)	2 ppm (1.6 mg/m^3)	2 ppm (1.6 mg/m^3)	2 ppm (1.6 mg/m^3)	1 ppm (0.8 mg/m^3)	1 ppm (0.8 mg/m^3)
AEGL-2 (Disabling)	95 ppm (78 mg/m^3)	55 ppm (45 mg/m^3)	39 ppm (32 mg/m^3)	10 ppm (8 mg/m^3)	7 ppm (6 mg/m^3)
AEGL-3 (Lethal)	170 ppm (139 mg/m^3)	94 ppm (77 mg/m^3)	67 ppm (55 mg/m^3)	33 ppm (27 mg/m^3)	24 ppm (20 mg/m^3)

HUMAN DATA-

NO EXPOSURE PARAMETERS
(CONCENTRATION AND TIME)

IRRITATION:

HEADACHE
DIZZINESS
OCULAR IRRITATION
NAUSEA
VOMITING
IRRITANT COUGH
SICKENING-SWEET TASTE

CLINICAL LATENCY PERIOD: ≤24 HOURS

PULMONARY SYMPTOMS:

COUGH ACCOMPANIED BY EXPECTORATION
SENSATION OF PAIN OR TIGHTNESS OF CHEST
SHORTNESS OF BREATH
CHOKING SENSATION

CLINICAL FINDINGS:

HEMOCONCENTRATION
RALES
PULMONARY EDEMA

Summary of Proposed AEGL Values for Phosgene

Classification	30-min	1-hr	4-hr	8-hr	Endpoint (Reference)
AEGL-1 (Nondisabling)	0.08 ppm (0.3 mg/m^3)	0.04 ppm (0.2 mg/m^3)	0.01 ppm (0.04 mg/m^3)	0.005 ppm (0.02 mg/m^3)	No-effect-level for increased LFP in rats*(Hatch et al., 1986)
AEGL-2 (Disabling)	0.16 ppm (0.7 mg/m^3)	0.08 ppm (0.3 mg/m^3)	0.02 ppm (0.08 mg/m^3)	0.01 ppm (0.04 mg/m^3)	No-effect-level for severe pneumonitis in rats (Gross et al., 1965)
AEGL-3 (Lethality)	0.7 ppm (2.9 mg/m^3)	0.3 ppm (1.3 mg/m^3)	0.08 ppm (0.3 mg/m^3)	0.04 ppm (0.2 mg/m^3)	50-minute rat LC_{50} (Zwart et al., 1990)

* also:mouse, hamster, guinea pig, rabbit

AEGL-2 FOR PHOSGENE (ppm [mg/m^3])				
AEGL Level	30-min	1-hr	4-hr	8-hr
AEGL-2	0.16 [0.7]	0.08 [0.3]	0.02 [0.08]	0.01 [0.04]

Species: Rat
Concentration: 0.8 ppm phosgene
Time: 1 hour
Endpoint: No-effect-level for severe pneumonitis; 1 Hour LOEL for moderate pneumonitis
Reference: Gross et al., 1965

n = 1

Uncertainty Factor = 10

Interspecies = 3 (little species variability observed for both lethal and non-lethal effects)

Intraspecies = 3 (mechanism is irritation and binding to macromolecules and is not expected to vary greatly between individuals)

Supporting data: Increased LFP in rats, mice, and hamsters exposed to 0.2 ppm phosgene for 4 hr (Hatch et al., 1986)

AEGL-1 FOR PHOSGENE (ppm [mg/m^3])				
AEGL Level	30-min	1-hr	4-hr	8-hr
AEGL-1	0.08 [0.3]	0.04 [0.2]	0.01 [0.04]	0.005 [0.02]

Species: Rat, mouse, hamster, guinea pig, rabbit
Concentration: 0.1 ppm phosgene
Time: 4 hours
Endpoint: No-effect-level for increased LFP
Reference: Hatch et al., 1986

n = 1

Uncertainty Factor = 10

Interspecies = 3 (little species variability observed for both lethal and non-lethal effects)

Intraspecies = 3 (mechanism is irritation and binding to macromolecules and is not expected to vary greatly between individuals)

(Is an AEGL-1 appropriate for phosgene?)

Summary of Proposed AEGL Values for Phosgene					
Classification	30-min	1-hr	4-hr	8-hr	Endpoint (Reference)
AEGL-1 (Nondisabling)	0.08 ppm	0.04 ppm	0.01 ppm	0.005 ppm	No-effect-level for increased LFP in rats* (Hatch et al., 1986)
AEGL-2 (Disabling)	0.16 ppm	0.08 ppm	0.02 ppm	0.01 ppm	No-effect-level for severe pneumonitis in rats (Gross et al., 1965)
AEGL-3 (Lethality)	0.7 ppm	0.3 ppm	0.08 ppm	0.04 ppm	50-minute rat LC_{50} (Zwart et al., 1990)

*also mouse, hamster, guinea pig, rabbit

ACGIH TLV (ACGIH, 1991): **0.1 ppm**

NIOSH IDLH (NIOSH, 1994): **2 ppm**

NIOSH STEL (NIOSH, 1994): **0.2 ppm (15 min)**

OSHA PEL (NIOSH, 1994): **0.1 ppm (8 hr)**

ERPG, 1-hour (AIHA, 1989):

ERPG-1: **Not Appropriate**
ERPG-2: **0.2 ppm**
ERPG-3: **1 ppm**

AEGL-3 FOR PHOSGENE (ppm [mg/m^3])				
AEGL Level	30-min	1-hr	4-hr	8-hr
AEGL-3	0.7 [2.9]	0.3 [1.3]	0.08 [0.3]	0.04 [0.2]

Species: Rat
Endpoint: ⅓ of 50 minute LC_{50}
Reference: Zwart et al., 1990
n = 1

Uncertainty Factor = 10

Interspecies = 3 (little species variability observed for both lethal and non-lethal effects)

Intraspecies = 3 (mechanism is irritation and binding to macromolecules and is not expected to vary greatly between individuals)

Supporting data: Severe pulmonary edema and body weight loss in rats exposed to 1 ppm phosgene for 1 hour (Franch and Hatch, 1986; Ehrlich et al., 1989).

~ PHOSGENE ~
Human Experience

Prof. Dr. Werner F. Diller
Univ. Duesseldorf - Germany
Occupational Health Physician

Human Volunteers - Odor

Concentration (ppm)	Odor Threshhold	Author
0.1	Perception	Schley (34)
0.1 - .25	Recognition	Schley (34)
1.25 - 0.25	Recognition	Potts (45)
0.4	Recognition	Wells (38)
0.5 - 2.0	Threshhold	Leonardos (68)
1.0	Threshhold	Patty (65)
1.5	Recognition	Wells (38)
5.6	Perception	US Bureau Mines (21)

Diller and Zante, 1982

Human Volunteers - Irritation

Concentration (ppm)	Irritation	Author
3.1	Throat	US Mines (21)
4.0	Eyes	ibid
4.8	Cough	ibid
10.0	Severe eye & airways	Vedder (25)

Diller and Zante, 1982

Human Experience - Lethality

Dose (ppm x min.)	Effect	Author
150 - 180	Lethal	Starkenstein (29)
225 - 250	Lethal	Becker - Schumann (14)
300 (10 ppm x 30 min)	Lethal	Zielhuis (70)
560 (12.5 ppm x 30 - 60 min)	Dangerous to Life	Flury and Zernick (31)
750 (25 ppm x 30 min)	Life - threatening	NIOSH (77)
800 (400 ppm x 2 min)	LCT_{50}	Chasis (44)
1130	Lethal	Locket (57)
1250	LCT_{LO}	Prentiss (37)

Diller and Zante, 1982

Effect of Phosgene Exposure in Humans

EPA Table 2 & 4

Effect	Phosgene Exposure
Odor Perception	> 0.4 ppm
Odor Recognition	> 1.5 ppm
Eye, Nose, Throat, & Bronchial Irritation	> 3.0 ppm
Initial Lung damage	> 30 ppm x min.
Clinical Pulmonary Edema	> 150 ppm x min.
LCT_{LO}	~ 300 ppm x min.
LCT_{50}	~ 500 ppm x min.
LCT_{100}	~ 1,300 ppm x min.

Comparison of Draft 8 hour AEGLs w/ ACGIH "Threshold Limit Value"

AEGL 1 (8 hr) Discomfort	0.005 ppm	TLV (8 hr) 0.1 ppm
AEGL 2 (8 hr) Disability	0.01 ppm	
AEGL 3 (8 hr) Lethality	0.04 ppm	

Suggested derivation of AEGLs from TLV

AEGL - 1 (8 hr)	0.05 ppm	(½ TLV)
AEGL - 2 (8 hr)	0.2 ppm	(2 x TLV)
AEGL - 3 (8 hr)	0.5 ppm	(5 x TLV)

Scaling of TLV derived AEGLs

Classification	30 min (ppm)	1 hour (ppm)	4 hours (ppm)	8 hours (ppm)	Dose (ppmxMin)
AEGL-1	0.8	0.4	0.1	0.05	24
AEGL-2	3.2	1.6	0.4	0.2	< 100
AEGL-3	8.0	4.0	1.0	0.5	< 240

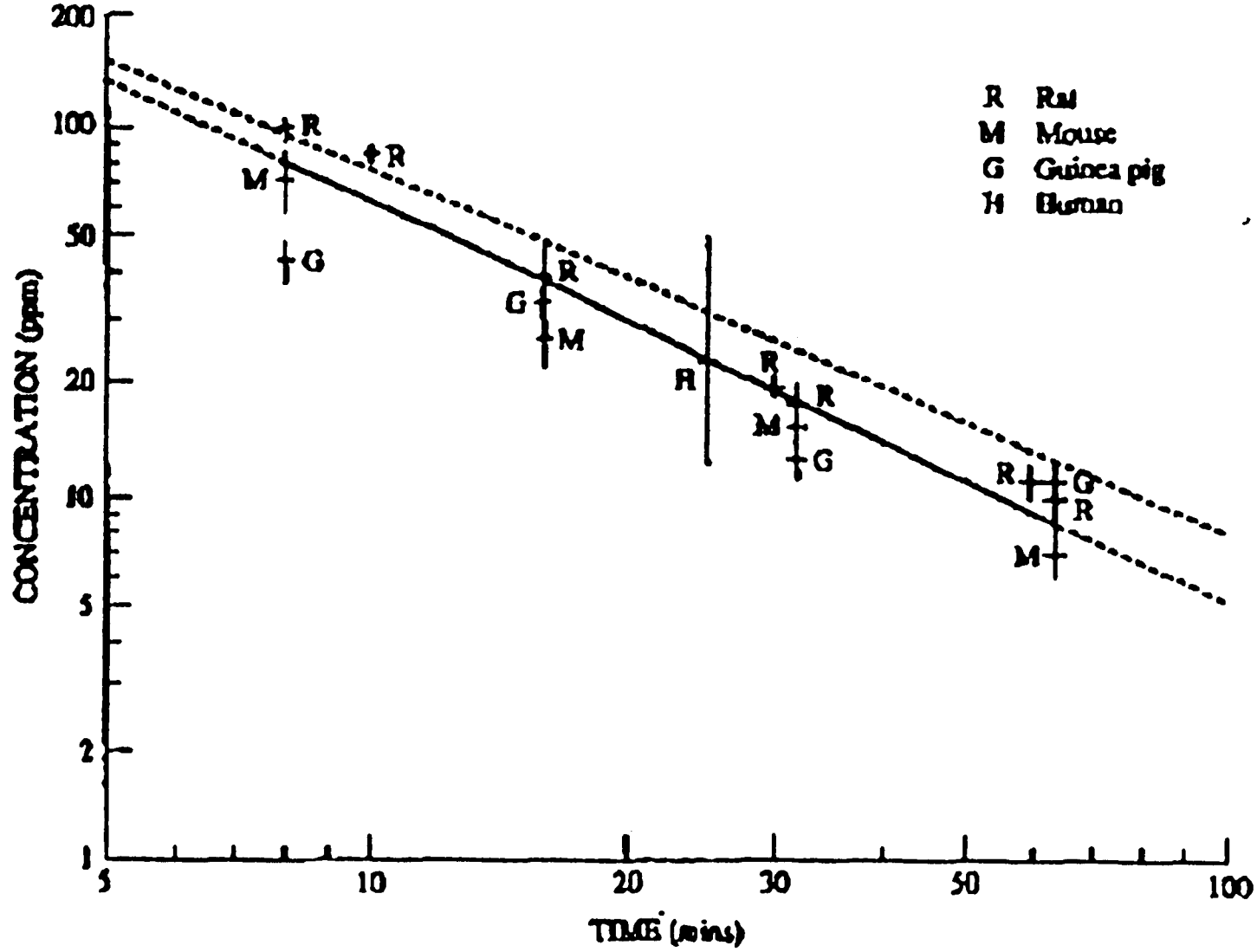

Figure 2. Concentration-time plots of median lethal concentration results of studies considered to be appropriate for derivation of a probit equation for phosgene.

CHEMICAL MANUFACTURERS ASSOCIATION

September 22, 1997

Paul S. Tobin, Ph.D.
Designated Federal Officer
National Advisory Committee/AEGL
U.S. Environmental Protection Agency
Mail Stop: 7406
401 M Street, S.W.
Washington, D.C. 20460

RE: Phosgene AEGL

Dear Mr. Tobin:

This letter is submitted on behalf of the Chemical Manufacturers Association Phosgene Panel (Panel) in response to the draft document proposing Acute Exposure Guideline Levels (AEGL) for phosgene.[1] While the Phosgene Panel appreciates the efforts of the U.S. Environmental Protection Agency and the National Advisory Committee in addressing the acute toxicity issues associated with phosgene, the Panel does not believe the proposed AEGL values are appropriate. The reasons are set forth below.

The Panel enlisted the efforts of the member company toxicology and industrial hygiene representatives to review the AEGL draft document (NAC/Pro Draft 3: 8/97). One of the major concerns with the proposed AEGL values is the application of conservative uncertainty factors in deriving them. The Panel believes that such conservative uncertainty factors are unwarranted due to the large number of scientific studies on phosgene which are currently available. The animal acute toxicity studies on phosgene are abundant, and the number of species tested is diverse. Based on this extensive data set, the Panel believes the uncertainty factors should be reduced resulting in higher, yet still appropriately protective, AEGL values.

According to the definition of AEGL-1 as described in the AEGL draft document, it is predicted that exposure to a substance at or above the AEGL-1 would result in discomfort (including mild odor, taste, or other sensory irritation) for the general population. Instead of using these referenced symptoms of discomfort for the

[1] Members of the Phosgene Panel include: Arco Chemicals Co.; BASF Corp.; Bayer Corp.; The Dow Chemical Co.; DuPont Chambers Works; GE Plastics; PPG Industries, Inc.; Rhone-Poulenc [illegible] Rubicon, Inc.; Van DeMark Chemical Co., Inc.; Zeneca Ag Products.

determination of AEGL-1 values for phosgene, the AEGL draft document references the use of increased Lavage Fluid Protein (LFP) as applied in Hatch *et al.* (1986)[2]. The use of LFP in establishing AEGL-1 values for phosgene is not appropriate because it deviates from the AEGL-1 definition (See attached Slide 4). Because of the discrepancy in using LFP as the criterion, the Panel believes it is inappropriate for the AEGL Committee to establish AEGL-1 values at this time.

The Panel agrees with the Committee in using the Gross *et al.* (1965)[3] study for development of the AEGL-2 values. The starting point for the AEGL-2 1-hour value is reasonable; however, the starting points for the AEGL-2 30 minute, 4-hour, and 8-hour values should be more directly linked to the Gross *et al.* data, rather than the *Concentration* x *time* ("Haber's Law") extrapolation from the AEGL-2 1-hour value. The response (i.e., the concentration which yields pneumonitis) does not appear to follow the simple *Concentration* x *time* relationship from one hour to eight hours of exposure. For example, although 0.8 ppm exposure causes a slight response after one hour, a similar slight to moderate response was seen after four to six hours of exposure to 0.5 ppm to 2.0 ppm. Haber's Law predicts a more severe response at four to eight hours than was observed by Gross *et al.*

The Panel believes it is more appropriate to establish AEGL values which are based on a ten Berge (1986)[4] extrapolation from 1 to 8 hours, because they appear to fit Gross' data better than a *Concentration* x *time* extrapolation at time points beyond one to two hours. The scaling equation developed by ten Berge has been used by the AEGL Committee in the draft document "Acute Exposure Guideline Levels for Phosgene" (NAC/ProDraft 2: 2/97). The following are the Panel's proposed AEGL-2 values (without an uncertainty factor applied) for preventing serious pneumonitis:

AEGL-2			
30 min	1-hour	4-hours	8-hours
2.4 ppm	0.8 ppm	0.4 ppm	0.28 ppm

As mentioned earlier, the Panel believes the available scientific data is sufficient enough to reasonably justify reducing the uncertainty factor by 3x for both the AEGL-2 and AEGL-3 values. The 3x uncertainty factor for interspecies differences is unnecessary because of the comparable response in humans to phosgene exposure. This uncertainty factor reduction results in 3x and 10x uncertainty factors for the AEGL-2 and AEGL-3, respectively (See attached Slides 7,10 and 11). Using these uncertainty

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[2] Hatch, G.E., Slade, R., Stead, A.G., and Graham, J.A. 1986. Species comparison of acute inhalation toxicity of ozone and phosgene. J. Toxico. Environmental Health 19: 43-53.
[3] Gross, P., Rinehart, W.E., and Hatch, T. 1965. Chronic pneumonitis caused by phosgene. Arch. Environ. Health. 10: 768-775.
[4] ten Berge, W.F., Zwart, A., and Appelman, L.M. 1986. Concentration-time mortality response relationship of irritant and systematically acting vapors and gases. J. Hazardous Materials 13: 301-309.

factors, the Panel proposes the following AEGL values for consideration by the AEGL Committee:

Proposed AEGL Values				
	30 min	1-hour	4-hour	8-hour
AEGL-1	N/A	N/A	N/A	N/A
AEGL-2	0.80 ppm	0.27 ppm	0.13 ppm	0.09 ppm
AEGL-3	2.2 ppm	1.1 ppm	0.28 ppm	0.14 ppm

N/A = Not Applicable

These values are consistent with the one hour American Industrial Hygiene Association Emergency Response Planning Guidelines (ERPG) which are cited in the AEGL draft document (See attached Slide 12). The ERPG-2 and ERPG-3 values cited are 0.2 ppm and 1 ppm, respectively. In addition, while the Panel acknowledges that the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLV) are established for a different purpose, it is useful to consider that the Panel's proposed AEGL-2 8-hour value is comparable to the current ACGIH TLV of 0.1 ppm as a time weighted average.

The Phosgene Panel appreciates the opportunity to provide comments on the AEGL draft document. We understand that the AEGL Committee meeting will be held in Washington, D.C. on September 23, 1997. The Phosgene Panel will be represented at that meeting by two industry members. Also in attendance will be Werner F. Diller, M.D. Professor Diller is an internationally renowned expert in the field of occupational medicine as it relates to phosgene exposure. He has published numerous articles on this subject, some of which are listed in the references for the draft AEGL document.

In the meantime, we look forward to meeting with you at the AEGL Committee meeting, and appreciate your consideration of the Panel's comments. Enclosed is a copy of the slides which will be presented at the September 23rd meeting, for your information. If you have any questions, please contact Chris Trent, Manager of the Phosgene Panel, at (703) 741-5627.

Sincerely,

Courtney Price /cmt

Courtney M. Price
Vice President, CHEMSTAR

Enclosure

PRESENTATION SLIDES

Phosgene AEGLs

T. D. Landry, Ph.D., D.A.B.T.
Chemical Manufacturers Association
CHEMSTAR Phosgene Panel

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CHEMSTAR Phosgene Panel

Member Companies:

ARCO Chemicals, BASF Corp., Bayer Corp., Dow Chemical, DuPont, GE Plastics, PPG Industries, Rhone-Poulenc Ag Co., Rubicon, Inc., Van DeMark Chemicals, Zeneca Ag Products

Panel Manager: Ms. Chris Trent

Commenters include:

M.Barmasse, D.Branson, H. Burleigh-Flayer, T.Harbourt, W.Hartgrove, K.Kiestler, G.Kennedy, D.Klonne, R.Leonard, J.P.Lyon, R.Parod, J.Shepherd, R.N.Shiotsuka, and G.Wright.

Phosgene AEGLs

- Important due to volatility and acute toxicity
- Appreciate the efforts of the AEGL committee to carefully assess phosgene
- AEGL document (NAC/Pro Draft 3:8/97) was well written and thoughtfully prepared

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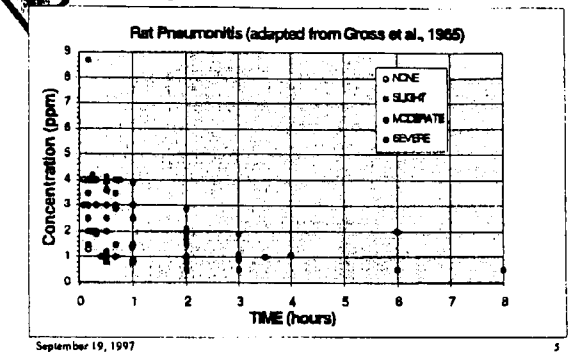
Phosgene AEGL1

- ...to prevent "notable discomfort"... airborne concentrations below AEGL1 "could produce mild odor, taste, or other sensory irritation."
- Increased Lavage Fluid Protein does not fit the AEGL1 definition

Phosgene AEGL1

- No increase in LFP in mice, rats, hamsters, guinea pigs, or rabbits exposed to 0.1 ppm for 4 hours
  - 10x uncertainty factor is conservative based on number of species tested and occupational exposure data
- AEGL1 values should be "Not Applicable"

Phosgene AEGL2



- Haber's rule does not apply well to these data- it implies a 16x difference (0.5 hr vs 8 hr)
- "ten Berge" extrapolation implies a 4x difference from 0.5 to 8 hours (square root of 16).

Assessment of Gross et al.: pneumonitis study in rats

Time (hours)	Draft NOEL	Time Specific "NOEL"	ten Berge extrapolation
0.5	1.6 ppm	**2.4 ppm** (0.5 hr avg)	1.1
1	0.8 ppm	**0.8 ppm**	(0.8 ppm)
4	0.2 ppm	1.1 ppm (one rat)	**0.40**
8	0.1 ppm	(no suitable data)	**0.28**

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- 2.4 ppm is for "Slight" and "Moderate" pneumonitis.
- 0.8 ppm is the value selected in AEGL draft.
- 0.40 and 0.28 are "ten Berge" extrapolations from 0.8 - one hour.

Phosgene AEGL2

- Animal acute toxicity studies are abundant
  - mice, rats, guinea pigs, hamsters, rabbits, dogs, sheep, goats, cats, monkeys ("non-lethal")
  - type and sequence of effects are similar in humans and experimental animals
- Uncertainty Factors
  - Interspecies (3x) is not warranted
  - Intraspecies (3x) appears reasonable

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◆proposal: 1-hour AEGL2, utilizing 3x intraspecies uncertainty factor (UF).

0.8 ppm / 3 (UF) = 0.27 ppm

AIHA ERPG2 = 0.2 ppm

Phosgene AEGL3

- Animal acute toxicity studies are abundant, but quality varies
  - mice, rats, guinea pigs, rabbits, dogs, sheep, goats, cats, monkeys (lethality studies)
  - little species variability

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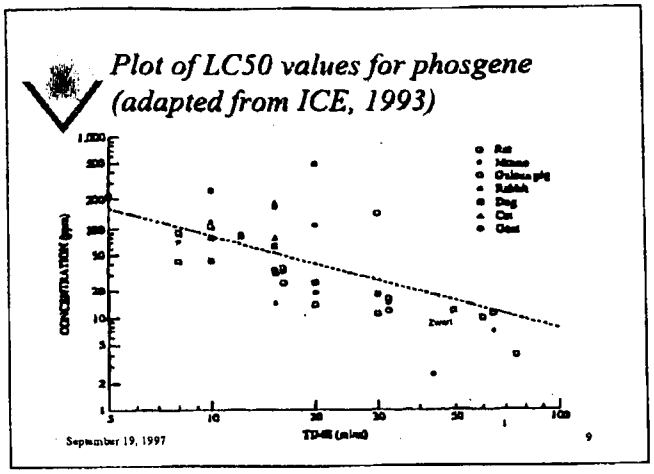

- The regression analysis combines studies of acceptable quality standards.
- Zwart data (as used by AEGL committee) was added to the figure, and fits well with the regression analysis
- Human data were excluded due to EPA policy of not using these wartime data (though value was consistent with the data shown).
- Institution of Chemical Engineers (1993). Phosgene Toxicity, Warwickshire, UK.

Phosgene AEGL3

- Use of 3 x 10 = 30 fold Uncertainty Factor yields numbers far below the LC50 plotted line which includes many species

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- The first 3x of the 30x is intended to be sure that lethality is avoided
- The 3x UF for interspecies variability is unnecessary, therefor 10x UF is suggested.

Phosgene AEGLs

- AEGL1: "Not Applicable" to phosgene
- AEGL2 from Gross *et al.* (1965)
  - time specific "NOEL" for 0.5 and 1 hours
  - "ten Berge" extrapolation for 4 and 8 hours
- AEGL2 and AEGL3
  - 3x and 10x Factors (rather than 10x and 30x) are consistent with the animal data

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CMA Phosgene Panel's AEGL proposals

	30 min	1 hour	4 hour	8 hour
AEGL 1	NA	NA	NA	NA
AEGL 2	0.80 ppm	0.27 ppm	0.13 ppm	0.09 ppm
AEGL 3	2.2 ppm	1.1 ppm	0.28 ppm	0.14 ppm

(NA = Not Applicable)

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- 0.09 ppm for 8 hours approximates the TLV.
- 0.14 ppm for 8 hours = 67 ppm.min, this is probably conservative (low) due to the C*t (Haber's rule) extrapolation.
- AIHA ERPG-1 = Not Applicable
  ERPG-2 = 0.2 ppm (one hour)
  ERPG-3 = 1 ppm (one hour)
- The above are appropriate for emergency response preparedness planning.
- Draft AEGL committee proposals (NAC/Pro Draft 3:8/97) are overly conservative based on available animal and human data.
- Consider presentation by Dr. Diller to help assess CMA proposed values.

PROPYL CHLOROFORMATE

- **MOUSE (SWISS-WEBSTER MALE): 30 MIN. RD_{50} = 83.5 PPM**
  (Carpenter, 1982)

  NO EVIDENCE OF PULMONARY EFFECTS

PPM	MORTALITY
25	0/4
50	1/4
75	2/4
100	0/4

- **RAT (CHARLES RIVER MALE & FEMALE):1-HR. LC_{50} = 410 PPM**
  (Bio-test, 1970)

  NOEL FOR ALL EFFECTS (INCLUDING DEATH): 249 PPM

- **MOUSE: 1-HR. LC_{50} = 319 PPM**
  (Kirk-Othmer, 1978)

ISOPROPYL CHLOROFORMATE

- **MOUSE (SWISS-WEBSTER MALE): 30 MIN. RD_{50} = 104 PPM**
  (Carpenter, 1982)

PPM	MORTALITY
50	1/4
75	3/4
100	4/4
200	4/4
500	4/4

- **MOUSE (SWISS-WEBSTER MALE): 15 MIN. RD_{50} = 375 PPM**
  (Anderson, 1984)

  LC_{50} ESTIMATE: 283-345 PPM

PPM	MORTALITY
141	0/4
283	2/4
345	2/4
730	4/4

- **RAT (CHARLES RIVER MALE & FEMALE):1-HR. LC_{50} = 300 PPM**
  (Bio-test, 1970)

- **RAT (ADERLY PARK MALE & FEMALE)**
  (Gage, 1970)

5 ppm	unknown duration	No effects
20 ppm	20 6-hr exposures	Nasal irritation
50 ppm	11 6-hr exposures	Respiratory difficulty, weight loss, death (1 animal)
200 ppm	5 hr	Death (2 males)

Isopropyl Chloroformate (Con't.)

- **RAT (SPRAGUE DAWLEY MALE & FEMALE)**
  (Collins & Proctor, 1984)

  Repeated exposure: 6 hr/day for 5 days

22, 42, and 86 ppm	**Concentration-related increase in lung weight; histopathology**
86 ppm	**Death**

METHYL CHLOROFORMATE

- **RAT (SPRAGUE-DAWLEY MALE): 1-HR LC_{50} = <728 PPM**
  (Warf, 1971)

- RAT (CHARLES RIVER): **1-HR LC_{50} = 163 PPM**
  (Bio-test, 1975)

- RAT: **1-HR LC_{50} (MALE) = 88 PPM**
  1-HR LC_{50} (FEMALE) = 103 PPM
  (Vernot et al., 1977)

- RAT (FISCHER 344): **1-HR LC_{50} (MALE): 92-123 PPM**
  1-HR LC_{50} (FEMALE): 100-153 PPM

  NO-EFFECT-LEVEL: 26 PPM (Death and clinical signs)
  (Fisher et al., 1981)

- RAT (SPRAGUE-DAWLEY MALE & FEMALE):

  REPEATED EXPOSURE: 6 HR/DAY, 5 DAYS/WEEK, 4 WEEKS

NOEL:	0.38 ppm
Upper respiratory histopathology:	1.0 ppm
NOEL for death (includes histopath.):	3.1 ppm
Death:	8.8 ppm

(BASF, 1993)

- MOUSE (SWISS-WEBSTER MALE):.10 MIN. RD_{50} = 52.4 ppm

  LC_{25} = 50-75 ppm

  HEMORRHAGIC LUNG TISSUE AT NECROPSY: 125 PPM

  (Carpenter, 1982)

AEGL-2 FOR METHYL CHLOROFORMATE (ppm [mg/m^3])				
AEGL Level	30-min	1-hr	4-hr	8-hr
AEGL-2	0.36 [1.4]	0.24 [0.94]	0.13 [0.51]	0.09 [0.35]

Species: Rat
Concentration: 3.1 ppm
Time: 6 hr (6 hr/day, 5 days/week, 4 weeks)
Endpoint: No-effect-level for pulmonary pathology

n=2

Uncertainty Factors:
10 for interspecies variability
(data in limited number of species, most sensitive species not used)

3 for interspecies variability (irritation)

AEGL-3 FOR METHYL CHLOROFORMATE (ppm [mg/m^3])				
AEGL Level	30-min	1-hr	4-hr	8-hr
AEGL-3	1.2 [4.7]	0.87 [2.5]	0.43 [1.7]	0.31 [1.2]

Species: Rat
Concentration: 26 ppm
Time: 1 hr
Endpoint: No-effect-level for death

n=2

Uncertainty Factors:
10 for interspecies variability
(data in limited number of species, most sensitive species not used)

3 for interspecies variability (irritation)

PROPOSED AEGL VALUES FOR METHYL CHLOROFORMATE					
Classification	**30-min**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL-1 (Nondisabling)	-	-	-	-	**NA**
AEGL-2 (Disabling)	**0.36 [1.4]**	**0.24 [0.94]**	**0.13 [0.51]**	**0.09 [0.35]**	**No-effect-level for lung pathology in rats repeatedly exposed to 3.1 ppm (BASF, 1993)**
AEGL-3 (Lethality)	**1.2 [4.7]**	**0.87 [2.5]**	**0.43 [1.7]**	**0.31 [1.2]**	**No-effect-level for death in rats exposed to 26 ppm for 1 hr (Fisher et al., 1981)**

PROPYLENE OXIDE AEGLs

Jim Holler
Claudia M. Troxel

PROPYLENE OXIDE

- **PROPERTIES**
  Extremely flammable, highly volatile, colorless liquid

- **USES**
  Used in production of polyurethane foams and resins, propylene glycol, functional fluids, and propylene oxide-based surfactants
  Used as food fumigant, soil sterilizer, acid scavenger

- **PRODUCTION**
  Estimated that 3,575 - 3650 million pounds of propylene oxide will be produced in the U.S. in 1998.
  Worldwide annual capacity for propylene oxide production was estimated at 8.8 billion pounds on Jan 1, 1994

- **AVAILABLE DATA**

  Human exposure data sparse and inconclusive

  Inhalation toxicity studies in animals available

HUMAN DATA

- **SUBLETHAL EFFECTS**

Case-report: worker exposed to 589,000 ppm propylene oxide vapor for 10-15 min: eye and lung irritation, burning in chest, restlessness, headache, weakness, diarrhea, vomiting, unconsciousness

Odor threshold: Range of 10-200 ppm; odor is sweet, alcoholic in nature

Genotoxicity/Carcinogenicity: Inconclusive: good correlation between exposure and decreased DNA repair proficiency and hemoglobin adduction; no significant correlation between exposure and chromosomal aberrations or cancer

- Pero, R.W., et al. 1982. A reduced capacity for unscheduled DNA synthesis in lymphocytes from individuals exposed to propylene oxide and ethylene oxide.

  5 occupationally exposed workers exposure to estimated TWA of 0.6-12 ppm during 5 working days; some workers had short exposures to high concentrations (1000 ppm)

  Resulted in measurable decrease in DNA repair proficiency (measured unscheduled DNA synthesis following *in vitro* challenge with N-acetoxy-2-acetylaminofluorene in lymphocytes)

SUMMARY OF SUBLETHAL INHALATION DATA IN LABORATORY ANIMALS				
Species	Conc. (ppm)	Dur. (h)	Effects	References
Dog	1363	4	Highest concentration causing no mortality; Lacrimation, salivation, nasal discharge	Jacobson et al., 1956
Rat	2684	4	Highest concentration causing no mortality; Frequent movement and preening, nasal discharge, lacrimation, salivation, gasping	Jacobson et al., 1956
Rat	1277	4	No mortality; no clinical sings or gross pathology changes	NTP, 1985
Rat (M)	4050	4	Highest concentration causing no mortality; Lacrimation, eye irritation, sedation, piloerection, mucous discharge from nose and mouth, respiratory difficulty	Shell Oil Co., 1977
Rat (F)	3450	4	Highest concentration causing no mortality; Lacrimation, eye irritation, sedation, piloerection, mucous discharge from nose and mouth, respiratory difficulty	Shell Oil Co., 1977
Rat	600	6 hr/d, 5 d/wk	Transient restless behavior observed only during first 3 days of exposure, occasional salivation and piloerection noted	Dow Chemical Company, 1981
Rat	997	6 h/d, 10 d	Excessive lacrimation and eye irritation, sedation, piloerection, mucous discharge (frequently bloodstained), respiratory difficulty - All disappeared after 3 day of exposure	Shell Oil Company, 1977

SUMMARY OF SUBLETHAL INHALATION DATA IN LABORATORY ANIMALS, cont.				
Species	Conc. (ppm)	Dur. (h)	Effects	References
Mouse (M)	859	4	Highest concentration causing no mortality; Dyspnea; no compound-related effects at gross necropsy	NTP, 1985
Mouse (F)	387 859	4 4	1/5 died (not treatment-related); dyspnea; no compound-related effects at gross necropsy No mortality; dyspnea; no compound-related effects at gross necropsy	NTP, 1985
Mouse	98.5 196 487	6 h/d, 5d/wk, 2wk	No-effects Dyspnea Dyspnea, hypoactive	NTP, 1985
Mouse	31, 63, 125, 250, 500	6 h/d, 5 d/wk, 13 wk	No mortalities except one in 125 ppm group; no gross or microscopic changes observed in any groups	NTP, 1985
Guinea pig	16,000 8000 4000 2000	0.5 1 2 7	Highest concentrations/longest durations not causing mortality; Signs of toxicity in all groups: eye and nasal irritation, breathing difficulty, drowsiness, weakness	Rowe et al., 1956

DOGS

- Jacobson et al., 1956. The toxicity of inhaled ethylene oxide and propylene oxide vapors.

3 male, beagle dog/group exposed **to 1363, 2005, 2030, or 2481 ppm** PO for **4 hours**

Lacrimation, salivation and nasal discharge in all dogs

MALE DOGS EXPOSED TO PO FOR 4 HOURS		
Conc. (ppm)	Mortality (%)	Other Effects
1363	0/3 (0)	
2005	1/3 (33)	motor weakness
2030	2/3 (67)	motor weakness, pulmonary edema and congestion
2481	3/3 (100)	motor weakness, pulmonary edema and congestion

RATS

- Jacobson et al., 1956.

Groups of 10 white male rats exposed to **945, 1329, 2684, 3448, 4490, or 5254 ppm** PO for **4 hours**

Frequent movement and preening, clear nasal discharge, lacrimation, salivation, gasping which increased in intensity during exposure, and death
Necropsy: only distended stomach
Mortality in rats exposed to 3448 ppm or higher

- Shell Oil Company, 1977.

3 male and 3 female Wistar rats/group exposed to 0 or **997 ppm** PO for **6 h/d for 10 days**

No mortalities
Irritation : Excessive lacrimation and eye irritation, sedation, piloerection, mucous discharge (frequently bloodstained) from the nose and mouth, and respiratory difficulty that continued for several hours after exposure - all disappeared after 3 day of exposure
Microscopic changes: necrosis and inflammation of respiratory epithelium; epithelial proliferation and focal hyperplasia and metaplasia

- Dow Chemical Company, 1981.

10 male or 10 female SPF-reared rats/group exposed **0, 76, 149, 298, or 600 ppm** propylene oxide vapor for **6 h/d, 5 d/wk for 13 wks**

No mortalities
No effects in 76 ppm group
Transient restless behavior in 149, 298, and 600 ppm groups first 3 days of exposure; piloerection and salivation occasionally noted 600 ppm group
600 ppm: histopathology -degenerative and hyperplastic changes in the nose, including edema in the submucosa and focal atrophy and squamous metaplasia of the olfactory epithelium

- NTP, 1985

5 male or 5 female F344/N rats/group exposed to **0, 1277, 2970, 3794, or 3900 ppm** PO for 4 hours

Mortalities and toxic effects (red nasal discharge and dyspnea) occurred in all groups exposed to 2970 ppm or higher
No gross pathological changes in treated animals

MICE

- NTP, 1985.

Groups of 5 male and 5 female B6C3F$_1$ mice exposed to **0, 387, 859, 1102, 1277, or 2970 ppm** for **4 hours**

B6C3F$_1$ MICE EXPOSED TO PO FOR 4 HOURS			
Conc. (ppm)	Mortality (%)		Other Effects
	Males	Females	
387	0/5 (0)	1/5 (20)	dyspnea
859	0/5 (0)	0/5 (0)	dyspnea
1102	2/5 (40)	4/5 (80)	dyspnea
1277	2/5 (40)	5/5 (100)	dyspnea, sedation
2970	5/5 (100)	5/5 (100)	dyspnea, sedation, lacrimation

5 male or 5 female B6C3F$_1$ mice/group exposed to **0, 20.1, 47.2, 98.5, 196 or 487 ppm** PO for **6 h/d, 5 d/wk, for 2 wks.**

No mortalities

Dyspnea in 196 and 487 ppm groups, and 487 ppm groups were hypoactive

10 male and 10 female B6C3F$_1$ mice/group exposed to **0, 31, 63, 125, 250, or 500 ppm** PO for **6 h/d, 5 d/wk**, for **13 wks.**

No mortalities except 1 male 125 ppm mouse on Day 14

High dose groups had lower body wts.; no gross or microscopic compound-related changes

SUMMARY OF INHALATION LC_{50} DATA IN LABORATORY ANIMALS				
Species	Conc. (ppm)	Duration (h)	LC_{50} - Method of Calculation	Reference
Dog	1941	4	Probit analysis (calc. for document) (use with caution)	Jacobson et al., 1956
Rat	4000	4	Bliss-Finney method	Jacobson et al., 1956
Rat	3205	4	Probit analysis (calc. for document)	NTP, 1985
Rat	4197	4	Not given	Shell Oil Co., 1977
Mouse	1740	4	Bliss-Finney method	Jacobson et al., 1956
Mouse	1106	4	Probit analysis (calc. for document)	NTP, 1985

SUMMARY OF 4-HOUR LC_{50} and ESTIMATED LC_{01} VALUES FOR PROPYLENE OXIDE AND ETHYLENE OXIDE			
Species	LC_{50} (ppm)	LC_{01} (ppm)	Reference
Propylene Oxide			
Dog	1941	930	Jacobson et al., 1956
Rat	4000 3205	2280 1037	Jacobson et al., 1956 NTP, 1985
Mouse	1740 1106 1160[a]	624 275 451[a]	Jacobson et al., 1956 NTP, 1985
Ethylene Oxide			
Dog	960	120	Jacobson et al., 1956
Rat	1460 1741	628 922	Jacobson et al., 1956 Nachreiner, 1991
Mouse	835 623	406 264	Jacobson et al., 1956 NTP, 1987

[a] Probit analysis excluding the one female mouse death at 387 ppm, based on assumption that the death was not treatment-related

DERIVATION OF *n*

Empirical Derivation:

Rowe et al., 1956

Lethality data for rats exposed to 8000 or 16,000 ppm for 0.5 hour, 4000 or 8000 ppm for 1 hour, and 4000 or 8000 ppm for 2 hours

Estimates of LC_{50} values for each time point (but based on only two concentrations!) used in linear regression analysis of log time vs. log LC_{50}

$n = 1.7$

Other Alternative:

Use derived value of *n* for ethylene oxide because of similar mechanisms; ***n* = 1.1** (derived from rat 1- and 4-hour LC_{50} values)

- Direct alkylating agents that alkylate DNA and proteins
- Possess irritant properties
- Affect nervous system

AEGL-1 (ppm)			
30 minutes	1 hour	4 hours	8 hours
150	80	23	12

- **Reference:** Pero, R.W., et al. 1982. A reduced capacity for unscheduled DNA synthesis in lymphocytes from individuals exposed to propylene oxide and ethylene oxide.

- 5 occupationally exposed workers

- **Concentration/Time Selection/Rationale:**
  Exposure to estimated TWA of 0.6-12 ppm during 5 working days resulted in measurable decrease in DNA repair proficiency

- **Uncertainty Factors/Rationale:**
  Total uncertainty factor: NA (1)
  Interspecies: NA (1) - human data used
  Intraspecies: NA (1) - endpoint sensitive measure of exposure, change in endpoint not expected to affect health

- **Time scaling:** $C^n \times t = k$ where $n = 1.1$; based on similar mechanism of action of propylene oxide compared to ethylene oxide

SUPPORTING DATA FOR AEGL-1

AEGL-1 (ppm)			
30 minutes	1 hour	4 hours	8 hours
160	84	24	13

NTP, 1985

Mice exposed to 98.1 ppm for 6 h/d, 5 d/wk for 2 wks: no-effect-level (no dyspnea)

UF = 6

n = 1.1

AEGL-2 (ppm)			
30 minutes	1 hour	4 hours	8 hours
310	170	47	25

- **Reference:** Jacobson, K. H., et al. 1956. The toxicity of inhaled ethylene oxide and propylene oxide vapors.

- 10 white male rats

- **Concentration/Time Selection/Rationale:**
Exposure to 945 ppm for 4 hours resulted in frequent moving and preening, clear nasal discharge, lacrimation, salivation, and gasping

- **Uncertainty/Modifying Factors/Rationale:**
Total uncertainty/modifying factor: 20
  - Interspecies: 3 - although an uncertainty factor of 10 might be used, the total UF would drive the AEGL-2 values lower than those for ethylene oxide
  - Intraspecies: 3 - mechanism of toxicity appears to be irritation and other point-of-entry effects, not that of a metabolite
  - Modifying: 2 - sparse database; severity of toxic signs not stated

- **Time scaling:** $C^n \times t = k$ where $n = 1.1$; based on similar mechanism of action of propylene oxide compared to ethylene oxide

SUPPORTING DATA FOR AEGL-2

UF/modifying factor of 20:
interspecies: 3
intraspecies: 3
modifying factor: 2
n = 1.1 based on ethylene oxide derived n value

Dow Chemical Company, 1981.

Groups of 10 male and 10 female SPF-reared rats exposed to 600 ppm for 6 hours/day, 5 days/weeks for 13 weeks; transient restless behavior noted during first 3 days of exposure, disappearing thereafter; piloerection and salivation occasionally occurred

AEGL-2 (ppm)			
30 minutes	1 hour	4 hours	8 hours
290	150	44	23

NTP, 1985.
Groups of 5 male and 5 female F344/N rats exposed to 1277 ppm for 4 hours: no-effect-level

AEGL-2 (ppm)			
30 minutes	1 hour	4 hours	8 hours
430	230	65	34

Shell Oil Company, 1977.

Groups of 3 male and 3 female Wistar rats/group exposed to 997 ppm for 6 h/d for 10 days:

Lacrimation and eye irritation, sedation, piloerection, mucous discharge (frequently bloodstained) from the nose and mouth, and respiratory difficulty that continued for several hours after exposure - all disappeared after 3 day of exposure.

AEGL-2 (ppm)			
30 minutes	1 hour	4 hours	8 hours
480	250	72	38

AEGL-3 (ppm)			
30 minutes	1 hour	4 hours	8 hours
410	220	62	33

- **Reference:** Jacobson, K. H., et al. 1956. The toxicity of inhaled ethylene oxide and propylene oxide vapors.

- 10 white female mice

- **Concentration/Time Selection/Rationale:** Estimated 4-hour LC_{01} of 624 ppm in mice - conservative estimate of threshold for lethality

- **Uncertainty/Modifying Factors/Rationale:**
  Total uncertainty/modifying factor: 10

  Interspecies: 3 - mouse was most sensitive species

  Intraspecies: 3 - mechanism of toxicity appears to be irritation and other point-of-entry effects, not that of a metabolite

- **Time scaling:** $C^n \times t = k$ where $n = 1$; based on similar mechanism of action of propylene oxide compared to ethylene oxide

SUPPORTING DATA FOR AEGL-3

UF factor of 10: interspecies: 3
intraspecies: 3
n = 1.1 based on ethylene oxide derived n value

NTP, 1985. Rat 4-hour LC_{01} of 1037 ppm

AEGL-3 (ppm)			
30 minutes	1 hour	4 hours	8 hours
690	370	100	55

Jacobson et al., 1956. Dog 4-hour LC_{01} of 930 ppm

AEGL-3 (ppm)			
30 minutes	1 hour	4 hours	8 hours
620	330	93	50

NTP, 1985 Mouse 4-hour LC_{01} of 275 ppm

AEGL-3 (ppm)				
UF	30 minutes	1 hour	4 hours	8 hours
3	610	320	92	49
6	300	160	46	24

CANCER ASSESSMENT

- NTP, 1985: tumor response data on $B6C3F_1$ male mice, in which male mice exposed to 0, 200, or 400 ppm developed hemangiomas or hemangiosarcomas of the nasal cavity (0/50, 0/50, 10/50, respectively).

AEGL-3 (ppm)			
30 min	1 hour	4 hours	8 hours
2300	1200	340	180

- Supported by study Sellakumar et al., 1987:

12-week old male Sprague-Dawley rats
exposed 6 hours/day, 5 days/week to:
433 or 864 ppm for 30 days
1724 ppm for 8 days
Allowed to die naturally

No tumors observed

SUMMARY OF ALTERNATIVE AEGL-2 DERIVATIONS (ppm)					
Endpoint/Rationale/Reference	**UF**	**30 m**	**1 h**	**4 h**	**8 h**
Rats exposed to 945 ppm for 4 hours: irritation (Jacobson et al., 1956) STUDY CHOSEN	10	630	330	95	50
	20	**310**	**170**	**47**	**25**
	30	210	110	32	17
Rats exposed to 600 ppm for 6 h/d, 5 d/wk exhibited transient restlessness; salivation also noted (Dow Chemical Co., 1981)	10	570	300	87	46
	20	**290**	**150**	**44**	**23**
	30	190	100	29	15
Rats exposed to 997 ppm for 10 days exhibited irritation, sedation, mucous discharge, respiratory difficulty (Shell Oil Company, 1977)	10	950	510	140	77
	20	**480**	**250**	**72**	**38**
	30	320	170	48	26
No-effect level for rats exposed to 1277 ppm for 4 hours (NTP, 1985)	10	850	450	130	68
	20	**430**	**230**	**65**	**34**
	30	280	150	40	20

General Comments:	UF = 10	values exceed AEGL-3
	UF = 20	values chosen for actual or supporting study
	UF = 30	values approaches ethylene oxide

SUMMARY OF ALTERNATIVE AEGL-3 DERIVATIONS (ppm)					
Endpoint/Rationale/Reference	**UF**	**30 m**	**1 h**	**4 h**	**8 h**
Mouse 4-hour LC_{01} of 624 ppm (Jacobson et al., 1956) STUDY CHOSEN	3	1400	730	210	110
	6	690	370	100	55
	10	**410**	**220**	**62**	**33**
Rat 4-hour LC_{01} of 1037 ppm (NTP, 1985)	**10**	**690**	**370**	**100**	**55**
	20	350	190	50	28
Dog 4-hour LC_{01} of 930 ppm - use with caution (Jacobson et al., 1956)	**10**	**620**	**330**	**93**	**50**
	20	310	170	47	25
Mouse 4-hour LC_{01} of 275 ppm (NTP, 1985)	**3**	**610**	**320**	**92**	**49**
	6	300	160	46	24
General Comments: UF = 20 values approach AEGL-2					

SUMMARY OF NAC APPROVED AEGL VALUES FOR ETHYLENE OXIDE (ppm)					
AEGL	**30-Min.**	**1-Hr**	**4-Hr**	**8-Hr**	**Endpoint (Reference)**
1	NA	NA	NA	NA	NA
2	190	110	33	19	Rat: Nervous system effects, eye and respiratory irritation, dominant lethality when rats exposed to 1000 ppm for 4 hours ($UF^a = 30$; $n^b = 1.12$) (Embree et al., 1977)
3	360	200	63	35	Rat: Estimated 4-hour LC_{01} ($UF^c = 10$; $n = 1.12$) (Jacobson et al., 1956)

[a] Total uncertainty factor of 30:

intraspecies UF = 10 - 4-hour exposure at 1000 ppm is close to lethality threshold in rats and above lethality threshold in mice

interspecies UF = 3 - modes of action are likely to be similar between rodents and humans and systemic uptake of ethylene oxide is similar across species

[b] n = 1.12 based on rat lethality data

[c] Total uncertainty factor of 10:

intraspecies UF = 3 - for differences in intraspecies sensitivity

interspecies UF = 3 - rat was not the most sensitive species tested for lethality (mouse was)

CHEMICAL MANUFACTURERS ASSOCIATION

September 24, 1997

Paul S. Tobin, Ph.D.
Designated Federal Officer
National Advisory Committee/AEGL
U.S. Environmental Protection Agency (7406)
401 M Street, S.W.
Washington, D.C. 20460

Re: ***Proposed Propylene Oxide AEGL***

Dear Dr. Tobin:

This letter is submitted on behalf of the Chemical Manufacturers Association Propylene Oxide Panel (Panel) in response to the draft document proposing acute exposure guideline levels (AEGLs) for propylene oxide. Members of the Propylene Oxide Panel are ARCO Chemical Company, The Dow Chemical Company and Huntsman Corporation. While the Panel appreciates the efforts of the EPA and the National Advisory Committee in addressing the acute exposure issues associated with propylene oxide, the Panel does not believe that the appropriate supporting data and/or methodology were used to develop the proposed AEGL values. Reasons for these beliefs are presented below.

The Panel enlisted the efforts of the member company toxicologists and industrial hygienists to review the AEGL draft document (NAC/Pro Draft 1:9/97). In summary, the Panel does not agree with the end-points on which the proposed AEGL-1 and the proposed AEGL-2 are based, or the uncertainty factors that were applied in deriving the proposed AEGL-3.

In the case of the proposed AEGL-1, the Panel believes that "decreased DNA-repair proficiency" does not represent an end-point of "notable discomfort" as per the AEGL-1 definition. A more appropriate end-point would be that of mild irritation, disagreeable odor and/or slight lacrimation. In the case of the proposed AEGL-2, the cited effects observed in rats do not represent an "irreversible or other serious, long-lasting effect or impaired ability to escape" as per the AEGL-2 definition. A more appropriate end-point would be

that of severe irritation, severe lacrimation or dyspnea. In the case of the AEGL-3, the Panel agrees with the end-point selected, i.e. lethality, but disagrees with the uncertainty factors applied to the supporting toxicity data.

Unfortunately, due to the limited comment period at this stage in the process, the Panel is unable to provide the Committee with additional recommendations for revising the draft. We would, however, appreciate the opportunity to provide such recommendations and supporting details at some later date, preferably before the Committee publishes its proposal in the Federal Register, and certainly thereafter.

The Propylene Oxide Panel appreciates the opportunity to provide these comments on the draft AEGL document to the AEGL Committee in Washington, DC on September 24-25, 1997. If you have any questions, please call Marian K. Stanley, Manager of the Propylene Oxide Panel, at 703-741-5623.

Sincerely,

Courtney M. Price

Courtney M. Price
Vice President CHEMSTAR

cc: Propylene Oxide Panel/TRTG

ACRYLYL CHLORIDE AEGLs

Mark McClanahan
Claudia M. Troxel

ACRYLYL CHLORIDE

- **PROPERTIES**
  Pale, yellow, corrosive liquid
  Flammable
  Hydrolyzes to hydrochloric acid and acrylic acid
  Irritant, lacrimator

- **USES**
  Used as monomer and intermediate

- **PRODUCTION**
  No information

- **AVAILABLE DATA**
  Human exposure data limited to secondary sources
  Animal exposure data limited

HUMAN DATA

- **LETHAL AND SUBLETHAL EFFECTS:**

MSDS:

May be fatal as result of spasm, inflammation and edema of larynx and bronchi, chemical pneumonitis, and pulmonary edema

Listed as extremely destructive to mucous membranes of upper respiratory tract, eyes, and skin

Symptoms of exposure: burning sensation, wheezing, coughing, laryngitis, shortness of breath, headache, nausea, and vomiting

Secondary source:

Threshold of irritant action on mucous membranes: 0.65 ppm

SUMMARY OF LETHAL AND SUBLETHAL INHALATION DATA IN LABORATORY ANIMALS				
Species	Conc. (ppm)	Exp. Time	Effect	Reference
Mouse	25	2 h	LC_{50}	Izmerov et al., 1982
Rat	19	4 h	LC_{14}	Izmerov et al., 1982
Rat	100	2 h	lethargy, respiratory difficulty, pulmonary edema, no deaths	Gage, 1970
Rat	25	4 h	1/4 died; respiratory difficulty, eye irritation, incoordination, pulmonary edema and emphysema	Gage, 1970
Rat	5	5 x 5h	3/4 died; lethargy , respiratory difficulty, eye irritation, low temperature, weight loss, pneumonia	Gage, 1970
Rat	2.5	3 x 6h	1/8 died; weight loss, low temperature, pulmonary edema and inflammation	Gage, 1970

AEGL DERIVATIONS:

No AEGL values are proposed for acrylyl chloride:

Data inappropriate:

- Secondary sources

- Inhalation exposure study inappropriate:
  - nominal concentrations, not measured
  - purity of chemical not given
  - mixed with other chemicals for exposures

Cannot predict toxicity based on chemical reactivity:

$$CH_2CHCOCl + H_2O \rightarrow HCl + C_3H_4O_2$$

- 30 min-HCl LC_{50} values range from 2640-4700 ppm (2-hr LC_{50} approximately 660-1175 ppm)

- Rats exposed to 80 ppm acrylic acid for 20 x 6-hour exposures exhibited no toxic signs or irritation; high concentrations needed to produce irritancy

- 2-hr LC_{50} for acrylyl chloride reported to be 25 ppm

ACRYLYL CHLORIDE AEGLs

Mark McClanahan
Claudia M. Troxel

ACRYLYL CHLORIDE

- **PROPERTIES**
  Pale, yellow, corrosive liquid
  Flammable
  Hydrolyzes to hydrochloric acid and acrylic acid
  Irritant, lacrimator

- **USES**
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- **PRODUCTION**
  No information

- **AVAILABLE DATA**
  Human exposure data limited to secondary sources
  Animal exposure data limited

HUMAN DATA

- **LETHAL AND SUBLETHAL EFFECTS:**

MSDS:

May be fatal as result of spasm, inflammation and edema of larynx and bronchi, chemical pneumonitis, and pulmonary edema

Listed as extremely destructive to mucous membranes of upper respiratory tract, eyes, and skin

Symptoms of exposure: burning sensation, wheezing, coughing, laryngitis, shortness of breath, headache, nausea, and vomiting

Secondary source:

Threshold of irritant action on mucous membranes: 0.65 ppm

SUMMARY OF LETHAL AND SUBLETHAL INHALATION DATA IN LABORATORY ANIMALS				
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Rat	25	4 h	1/4 died; respiratory difficulty, eye irritation, incoordination, pulmonary edema and emphysema	Gage, 1970
Rat	5	5 x 5h	3/4 died; lethargy , respiratory difficulty, eye irritation, low temperature, weight loss, pneumonia	Gage, 1970
Rat	2.5	3 x 6h	1/8 died; weight loss, low temperature, pulmonary edema and inflammation	Gage, 1970

AEGL DERIVATIONS:

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$$CH_2CHCOCl + H_2O \rightarrow HCl + C_3H_4O_2$$

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- 2-hr LC_{50} for acrylyl chloride reported to be 25 ppm

BORON TRICHLORIDE

Mark McClanahan
Claudia M. Troxel

BORON TRICHLORIDE

- **PROPERTIES**
  Colorless gas at room temperature; fumes in moist air
  Hydrolyzes to produce heat, hydrochloric acid, and boric acid

- **USES**
  Manufacturing and purification of boron and diborane; catalyst for organic reactions; use in semiconductors; as a soldering flux

- **PRODUCTION**
  No information available

- **AVAILABLE DATA**
  No human exposure data
  Inhalation toxicity studies in animals limited to 2 studies

SUMMARY OF 1-HOUR LC_{50} VALUES IN RATS (Vernot et al., 1977)			
Species	**Conc. (ppm)**	**Exp. Time**	**Effect**
Rats - male	2541	1 h	LC_{50}
Rats - female	4418	1 h	LC_{50}

SUMMARY OF LETHAL AND SUBLETHAL BCl_3 INHALATION DATA IN LABORATORY ANIMALS
(Stokinger and Spiegl, 1953)

Species	Conc. (ppm)	Exp. Time	Effect
Cages used continuously for 7 hours			
Rats	20	7 h	10/10 died
Rats	50	2 x 7 h	10/10 died
Rats	85	2 x 7 h	3/10 died
Mice	20	7 h	10/10 died
Mice	50	2 x 7 h	10/10 died
Mice	85	2 x 7 h	10/10 died
Guinea pigs	20	7 h	0/10 died
Guinea pigs	50	2 x 7 h	0/10 died
Guinea pigs	85	2 x 7 h	0/10 died
Clean cages substituted every 2 hours during exposures			
Rats	20	2 x 7 h	0/10 died
Rats	50	2 x 7 h	0/10 died
Rats	100	2 x 7 h	0/10 died
Mice	20	2 x 7 h	0/15 died
Mice	50	2 x 7 h	0/15 died
Mice	100	2 x 7 h	14/15 died
Guinea pigs	20	2 x 7 h	0/10 died
Guinea pigs	50	2 x 7 h	0/10 died
Guinea pigs	100	2 x 7 h	10/10 died

Hydrolysis reaction of boron trichloride:

$$BCl_3 + 3H_20 \rightarrow H_3BO_3 + 3HCl$$

COMPARISON OF BCl_3 AND HCl LC_{50} VALUES IN MALE RATS			
Time (min)	**HCl (vapor) (ppm)**	**BCl_3 (ppm)**	**References**
5	40,989	-	Higgens et al., 1972
30	4700	-	Darmer et al., 1974
60	3124 -	2541 4418 (females)	Vernot et al., 1977

AEGL DERIVATIONS

Proposed AEGL values for boron trichloride based on NAC-approved values for hydrogen chloride:

- Lack of inhalation toxicity data
- One mole of boron trichloride theoretically hydrolyzes to form 3 moles of hydrogen chloride (HCl) in air
- AEGL values for boron trichloride are the NAC-approved values for hydrogen chloride divided by 3 to account for molar equivalents

AEGL-1 (ppm)				
30 minutes	1 hour	4 hours	8 hours	
1.8	1.8	1.8	1.8	HCl
0.6	0.6	0.6	0.6	BCl_3

DERIVATION OF HYDROGEN CHLORIDE AEGL-1:

- **Reference:** Stevens, B., et al. 1992. Respiratory effects from the inhalation of hydrogen chloride in young adult asthmatics.

- Ten, exercising young adult asthmatics

- **Concentration/Time Selection/Rationale:** Exposure to 1.8 ppm hydrogen chloride for 45 minutes resulted in a no-effect-level

- **Uncertainty Factors/Rationale:**
  Total uncertainty factor: NA (1)
  Interspecies: NA (1) - human data used
  Intraspecies: NA (1) - test subjects were sensitive population

- **Time scaling:** NA - values were flat-lined at the no-effect-level (mild irritant effects generally do not vary greatly over time and endpoint is inherently conservative

AEGL-2 (ppm)				
30 minutes	1 hour	4 hours	8 hours	
43	22	5.4	2.7	HCl
14.3	7.3	1.8	0.9	BCl_3

DERIVATION OF HYDROGEN CHLORIDE AEGL-2:

- **Reference:** Stavert , D.M., et al. 1991. Relative acute toxicities of hydrogen fluoride, hydrogen chloride, and hydrogen bromide in nose- and pseudo-mouth-breathing rats.

- 8 male Fischer 344 rats/exposure group

- **Concentration/Time Selection/Rationale:**
  Exposure to 1300 ppm HCl for 30 minutes produced severe nasal effects in nose-breathing animals; and severe pulmonary effects in mouth breathing animals

- **Uncertainty/Modifying Factors/Rationale:**
  Total uncertainty/modifying factor: 30
  - Interspecies: 3 - rats more sensitive
  - Intraspecies: 3 - mechanism of toxicity is irritation and is not expected to vary greatly between individuals
  - Modifying: 3 - relatively sparse database

- **Time scaling:** $C^n \times t = k$ where n = 1 (ten Berge et al., 1986)

AEGL-3 (ppm)				
30 minutes	1 hour	4 hours	8 hours	
210	100	26	13	HCl
70	33	8.7	4.3	BCl_3

DERIVATION OF HYDROGEN CHLORIDE AEGL-3:

- **Reference:** Wohlslagel, J., et al. 1976. Toxicity of solid rocket motor exhaust: effects of HCl, HF, and alumina on rodents and Vernot, E.H., et al., 1977.

- 10 male CFE (Sprague-Dawley derived) rats/ exposure group

- **Concentration/Time Selection/Rationale:**
  ⅓ the 1-hour LC_{50} value of 3124 ppm = 1041 ppm

- **Uncertainty/Modifying Factors/Rationale:**
  Total uncertainty factor: 10
  - Interspecies: 3 - rats more sensitive; ⅓ of no-effect-level for death conservative
  - Intraspecies: 3 - mechanism of toxicity is irritation and not expected to vary greatly between individuals

- **Time scaling:** $C^n \times t = k$ where n = 1 (ten Berge et al., 1986)

AEGL-3 (ppm)				
30 min.	1 hour	4 hours	8 hours	Based on:
170	85	21	11	Vernot et al., 1977
210	100	26	13	HCl
70	33	8.7	4.3	HCl ÷ 3

DERIVATION OF BORON TRICHLORIDE AEGL-3:

- **Reference:** Vernot, E.H., et al., 1977. Acute toxicity and skin corrosion data for some organic and inorganic compounds and aqueous solutions.

- 5 male Sprague-Dawley rats/exposure group

- **Concentration/Time Selection/Rationale:**
  ⅓ the 1-hour LC_{50} value of 2541 ppm = 847 ppm
  (females: 4418 ppm; combined: 3480 ppm)

- **Uncertainty/Modifying Factors/Rationale:**
  Total uncertainty factor: 10
  Interspecies: 3 - mechanism of toxicity not expected to vary across species; ⅓ of no-effect-level for death conservative
  Intraspecies: 3 - mechanism of toxicity appears to be irritation and not expected to vary greatly between individuals

- **Time scaling:** $C^n \times t = k$ where $n = 1$

AEGL-1 (ppm)				
30 minutes	1 hour	4 hours	8 hours	
1.8	1.8	1.8	1.8	HCl
0.6	0.6	0.6	0.6	BCl_3

AEGL-2 (ppm)				
30 minutes	1 hour	4 hours	8 hours	
43	22	5.4	2.7	HCl
14.3	7.3	1.8	0.9	BCl_3

AEGL-3 (ppm)				
30 minutes	1 hour	4 hours	8 hours	
210	100	26	13	HCl
70	33	8.7	4.3	BCl_3

ALLYL ALCOHOL AEGLs

Mark McClanahan
Claudia M. Troxel

ALLYL ALCOHOL

- **PROPERTIES**
  Colorless liquid
  Pungent, mustard-like odor

- **USES**
  Used in production of allyl esters (resins and plasticizers); intermediate in production of pharmaceuticals, organic chemicals; fungicide and herbicide; flavoring agent

- **PRODUCTION**
  No estimates on total production found

- **AVAILABLE DATA**
  Human exposure data limited
  Inhalation toxicity studies in animals available

HUMAN DATA

- **SUBLETHAL EFFECTS**

Odor threshold:

range of 1.4 - 2.1 ppm; mean of 1.8 ppm (AIHA, 1989)

Signs/symptoms:

Acutely exposed individuals may develop lacrimation, retrobulbar pain, blurred vision, severe irritation of mucous membranes with edema and excessive secretions

SUMMARY OF SENSORY RESPONSE TO ALLYL ALCOHOL DURING 5 MINUTE EXPOSURE (Dunlap et al., 1958)							
Conc. ppm	**No. Subjects**	**Eye Irritation**		**Nose Irritation**		**Olfactory Recognition**	
		Slight	**Moderate or >**	**Slight**	**Moderate or >**	**Slight**	**Moderate or >**
0.78	6	0	0	2	0	5	1
6.25	6	1	0	3	1	4	2
12.5	7	1	0	3	4	6	1
25.0	5	0	5	0	5	3	1

Notes: Short exposure duration - 5 minutes
Not stated if nominal or measured concentrations - probably nominal

Torkelson et al., 1959b

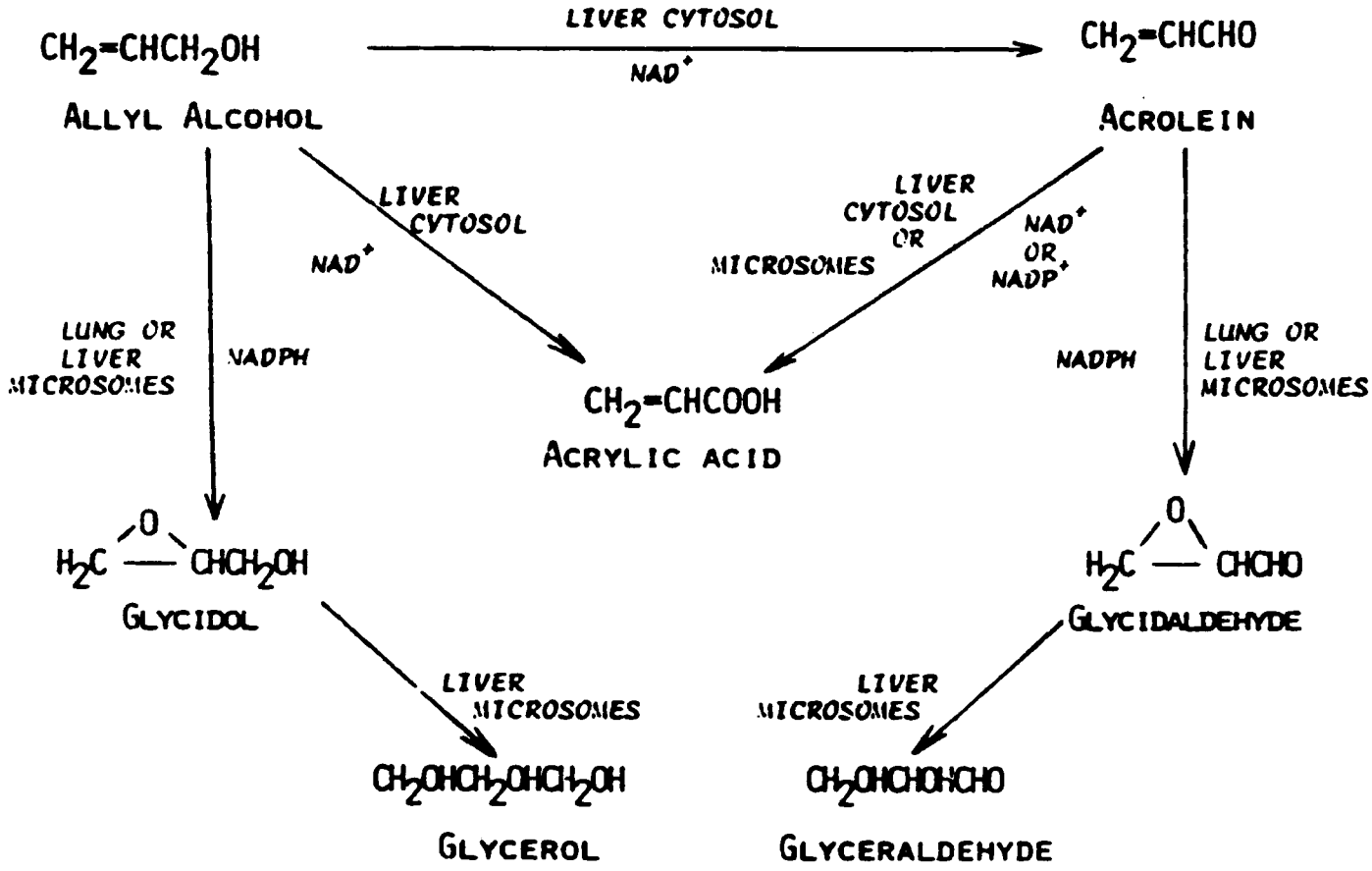
Ten volunteers exposed to 2 ppm allyl alcohol for 1-3 minutes reported distinct odor but no irritation

SUMMARY OF ACUTE LETHAL INHALATION DATA IN LABORATORY ANIMALS				
Species	**Conc. (ppm)**	**Exp. Time (h)**	**Effect**	**Reference**
Monkey	1000	4	1/1 died	McCord, 1932
Rat	1060 165 76	1 4 8	LC_{50}	Dunlap et al., 1958
Rat	200	1	0/10 died	Union Carbide, 1951
Rat	1000	0.5 1 2	1/6 died 4/6 died 6/6 died	Union Carbide, 1951
Rat	1000	1	4/6 died	Smyth and Carpenter, 1948
Rat	1000	3	6/6 died during exp.	McCord, 1932
Rat	200	2 x 7h	4/4 died by end 2 exp.	McCord, 1932
Rat	60 100 150	7h/d, 5d/wk, 60 exp	1/10 by 60th exp. 6/10 by 56 exp. 10/10 by 10 exp.	Dunlap et al., 1958
Mouse	200	1	0/10 died	Union Carbide, 1951
Mouse	500	0.5 1	0/10 died 4/10 died	Union Carbide, 1951
Mouse	1000	1 2 4	6/10 died 8/10 died 10/10 died	Union Carbide, 1951
Rabbit	200	1	0/10 died	Union Carbide, 1951
Rabbit	500	2 4	0/4 died 4/4 died	Union Carbide, 1951
Rabbit	1000	3.5 4.25	2/2 died during exp.: one at each exp. time	McCord, 1932

SUMMARY OF ACUTE LETHAL INHALATION DATA IN LABORATORY ANIMALS				
Species	**Conc. (ppm)**	**Exp. Time (h)**	**Effect**	**Reference**
Monkey	1000	4	1/1 died	McCord, 1932
Rat	1060 165 76	1 4 8	LC_{50}	Dunlap et al., 1958
Rat	200	1	0/10 died	Union Carbide, 1951
Rat	1000	0.5 1 2	1/6 died 4/6 died 6/6 died	Union Carbide, 1951
Rat	1000	1	4/6 died	Smyth and Carpenter, 1948
Rat	1000	3	6/6 died during exp.	McCord, 1932
Rat	200	2 x 7h	4/4 died by end 2 exp.	McCord, 1932
Rat	60 100 150	7h/d, 5d/wk, 60 exp	1/10 by 60th exp. 6/10 by 56 exp. 10/10 by 10 exp.	Dunlap et al., 1958
Mouse	200	1	0/10 died	Union Carbide, 1951
Mouse	500	0.5 1	0/10 died 4/10 died	Union Carbide, 1951
Mouse	1000	1 2 4	6/10 died 8/10 died 10/10 died	Union Carbide, 1951
Rabbit	200	1	0/10 died	Union Carbide, 1951
Rabbit	500	2 4	0/4 died 4/4 died	Union Carbide, 1951
Rabbit	1000	3.5 4.25	2/2 died during exp.: one at each exp. time	McCord, 1932

SUMMARY OF SUBLETHAL INHALATION DATA IN LABORATORY ANIMALS				
Species	**Conc. (ppm)**	**Exposure Duration**	**Effects**	**References**
Mouse	3.9	10 min	RD_{50}	Nielson et al., 1984
Mouse	2.5	10 min	RD_{50}	James et al., 1987
Mouse	2.4	6h/d, 4 d	Histopathological changes in upper respiratory epithelium (hyperplasia, inflammatory infiltrates, some epithelial cell desquamation) and olfactory epithelium (slight loss of isolated sensory cells)	Zissu, 1995

SUMMARY OF SUBLETHAL INHALATION DATA IN LABORATORY ANIMALS, cont.				
Species	**Conc. (ppm)**	**Exposure Duration**	**Effects**	**References**
Rat	1, 2, 5	7h/d, 5d/wk, 60 exp.	No observable adverse effects	Dunlap et al., 1958
Rat	20	7h/d, 5d/wk, 60 exp.	No adverse effects except decrease in body wt. gain	Dunlap et al., 1958
Rat	1, 5, 10, 20	8h/d for 60 exp. in 90 d	No observable adverse effects	Shell Chemical Corp., 1957
Rat	40	7h/d, 5d/wk, 60 exp.	Irritation (gasping, eye irritation, nasal discharge) disappeared after first few exp.; increased lung wt.	Dunlap et al., 1958
Rat	40	8h/d for 60 exp. in 90 d	Decreased growth, mild to moderate lung congestion	Shell Chemical Corp., 1957
Rat	60	8h/d for 60 exp. in 90 d	Lung congestion, increased kidney and lung wts., 1/10 died	Shell Chemical Corp., 1957
Rat, Guinea pig, Rabbit	7	7h/d, 5d/wk, 127-134 exp.	Reversible liver and kidney damage	Torkelson et al., 1959a


CH2=CHCH2OH
ALLYL ALCOHOL
LIVER CYTOSOL
NAD+
CH2=CHCHO
ACROLEIN
LIVER CYTOSOL
NAD+
LIVER CYTOSOL OR MICROSOMES
NAD+ OR NADP+
LUNG OR LIVER MICROSOMES
NADPH
CH2=CHCOOH
ACRYLIC ACID
NADPH
LUNG OR LIVER MICROSOMES
H2C — CHCH2OH
GLYCIDOL
H2C — CHCHO
GLYCIDALDEHYDE
LIVER MICROSOMES
LIVER MICROSOMES
CH2OHCH2OHCH2OH
GLYCEROL
CH2OHCHOHCHO
GLYCERALDEHYDE

Dunlap, M.K., et al. 1958. The toxicity of allyl alcohol.

10 male Long-Evans rats/group exposed to **0, 1, 2, 5, 20, 40, 60, 100, or 150 ppm** for **7 hours/day, 5 days/week, for 60 exposures**

SUMMARY OF EFFECTS	
Conc. (ppm)	**Effect**
1, 2, 5	No observable adverse effects
20	Only observable effect was decreased body weight
40	**Irritation: gasping, eye irritation, nasal discharge disappeared after first few exposures; increased lung wt.**
60	1/10 died after 4th exposure Irritation: gasping and muzzle rubbing first few exposures that disappeared thereafter; persistent eye discharge; increased lung and kidney wts.
100	6/10 died during first 46 days Similar signs of irritation
150	10/10 died by 10 exp. Necropsy: hemorrhagic livers, pale and spotted lungs, bloated G.I. tracts; slight congestion of liver and lungs

Shell Chemical Corporation. 1957. Initial submission: Review of allyl alcohol toxicity with cover letter dated 10/15/92.

Rats exposed to **0, 1, 2, 5, 20, 40, 60, 100, or 150 ppm** for **8 hours/day, 5 days/week, for 60 exposures in 90 days**

SUMMARY OF EFFECTS	
Conc. (ppm)	**Effect**
1, 2, 5, 20	No observable adverse effects
40	**Decreased growth; mild to moderate lung congestion**
60	1/10 died Mild to moderate lung congestion, increased lung and kidney wts.
100	All animals died by 32 exp.
150	All animals died by 2 exp. Necropsy: hemorrhagic livers, pale and spotted lungs, bloated G.I. tracts; slight congestion of liver and lungs

Union Carbide and Carbon Corporation. 1951. Initial submission: Letter from DuPont Chem to USEPA regarding a letter about toxicity studies with allyl alcohol with cover letter dated 10/15/92.

No mortality in groups of 10 **rats, mice or rabbits** exposed to **200 ppm** for **1 hour**.

GENERAL SUPPORTING DATA				
Species	Conc. (ppm)	Exp. Time (h)	Mortality	Reference
Rat	1000	0.5 1	1/6 4/6	Union Carbide, 1951
Rat	1060 165	1 4	*LC_{50} *LC_{50}	Dunlap et al., 1958
Mouse	500	0.5 1	0/10 4/10	Union Carbide, 1951
Rabbit	500	2 4	0/4 4/4	Union Carbide, 1951

* Target concentrations - although authors stated that actual concentrations ranged from 15-25% of nominal, actual measured concentrations not given

DERIVATION OF n

Empirical Derivation:

Dunlap et al., 1956

Rat 1-, 4-, and 8-hour LC_{50} values of 1060, 165, and 76 ppm, respectively. Regression analysis of log time vs. log LC_{50}

$n = 0.78$.

Note: Target concentrations presented in study - although authors stated that actual concentrations ranged from 15-25% of nominal, actual measured concentrations not given

Other Alternative:

"Default" value: $n = 2$ represents midpoint of reported values as referenced by ten Berge et al., 1986

Used $n = 2$ in time-scaling in AEGL derivations

AEGL-1 (ppm)			
30 minutes	1 hour	4 hours	8 hours
1.8	1.8	1.8	1.8

- **Reference:** AIHA 1989. Odor Thresholds for Chemicals with Established Occupational Health Standards.

- Mean odor detection threshold of 1.8 ppm (mean of 1.4 and 2.1 ppm)

- **Uncertainty Factors/Rationale:**
  Total uncertainty factor: NA (1)
  Interspecies: NA (1) - human data used
  Intraspecies: NA (1) - odor threshold

- **Time scaling:** NA - values were flat-lined at the no-effect-level (not dependent on length of exposure)

SUPPORTING DATA FOR AEGL-1

Torkelson et al., 1959b

Ten volunteers exposed to 2 ppm allyl alcohol for 1-3 minutes reported distinct odor but no irritation

Torkelson et al., 1959a

Rats, guinea pigs, rabbits, and dogs exposed to 2 ppm for 7 hours/day, 5 days/week for 28 exposures exhibited no adverse effects

Rats, guinea pigs, and rabbits exposed to 7 ppm for 7 hours/day, 5 days/week for 134 exposures only exhibited reversible liver and kidney damage

AEGL-2 (ppm)			
30 minutes	1 hour	4 hours	8 hours
15	11	5.3	3.7

- **Reference:** Dunlap, M.K., et al. 1958. The toxicity of allyl alcohol.

- 10 male Long-Evans rats/exposure group

- **Concentration/Time Selection/Rationale:** Exposure to 40 ppm for 7 hours/day caused irritation during the first few exposures that disappeared thereafter

- **Uncertainty/Modifying Factors/Rationale:**
  Total uncertainty factor: 10
  - Interspecies: 3 - does not appear to be much variation between species in their response to allyl alcohol
  - Intraspecies: 3 - mechanism of toxicity is most likely irritation and not expected to vary greatly between individuals

- **Time scaling:** $C^n \times t = k$ where $n = 2$ (represent midpoint of reported values as referenced by ten Berge et al., 1986)

SUPPORTING DATA FOR AEGL-2

AEGL-2 (ppm)			
30 minutes	1 hour	4 hours	8 hours
16	11	5.7	4.0

Shell Oil Corporation, 1957

Rats exposed to 40 ppm for 8 h/d, 5 d/wk for 60 exposures in 90 days - Mild to moderate lung congestion

UF = 10

n = 2

AEGL-3 (ppm)			
30 minutes	1 hour	4 hours	8 hours
28	20	10	7.1

- **Reference:** Union Carbide and Carbon Corporation. 1951. Initial submission: Letter from DuPont Chem to USEPA regarding a letter about toxicity studies with allyl alcohol with cover letter dated 10/15/92.

- Groups of 10 rats, mice, or rabbits

- **Concentration/Time Selection/Rationale:**
  NOEL for lethality in mice, rats, and rabbits exposed to 200 ppm for 1 hour

- **Uncertainty/Modifying Factors/Rationale:**
  Total uncertainty factor: 10
  - Interspecies: 3 - does not appear to be much variation between species in their response to allyl alcohol
  - Intraspecies: 3 - mechanism of toxicity is most likely irritation and not expected to vary greatly between individuals

- **Time scaling:** $C^n \times t = k$ where $n = 2$ (represent midpoint of reported values)

SUPPORTING DATA FOR AEGL-3

AEGL-3 (ppm)			
30 minutes	1 hour	4 hours	8 hours
50	35	18	13

Union Carbide, 1951

NOEL for death in mice exposed to 500 ppm for 0.5 hours

UF = 10

n = 2

AEGL-1 (ppm)			
30 minutes	1 hour	4 hours	8 hours
1.8	1.8	1.8	1.8

AEGL-2 (ppm)			
30 minutes	1 hour	4 hours	8 hours
15	11	5.3	3.7

AEGL-3 (ppm)			
30 minutes	1 hour	4 hours	8 hours
28	20	10	7.1

SUMMARY OF SUPPORTING/ALTERNATIVE AEGL-1 DERIVATIONS (ppm)						
Endpoint/Rationale/Reference	**UF**	***n***	**30 m**	**1 h**	**4 h**	**8 h**
Human volunteers exposed to 12.5 ppm for 5 minutes: nasal irritation (Dunlap et al. 1958)	3	2	1.7	1.2	0.60	0.43
TLV-TWA is 2 ppm; scaling from 5 minute study; not stated if measured concentration; below odor threshold						
Rats repeatedly exposed to 20 ppm for 7 hours: NOEL (Dunlap et al., 1958)	10	2	7.5	5.3	2.6	1.9
No AEGL-1 effects noted						

SUMMARY OF SUPPORTING/ALTERNATIVE AEGL-2 DERIVATIONS (ppm)						
Endpoint/Rationale/Reference	**UF**	***n***	**30 m**	**1 h**	**4 h**	**8 h**
Humans exposed to 25 ppm for 5 minutes experienced severe eye irritation (Dunlap et al., 1958)	1	2	10	7.2	3.6	2.6
	3	2	3.4	2.4	1.2	0.85
TLV-TWA is 2 ppm; scaling from 5-min study; not stated if measured concentration.						
Rats repeatedly exposed to 20 ppm for 7 hours: NOEL (Dunlap et al., 1958)	10	2	7.5	5.3	2.6	1.9
TLV-TWA is 2 ppm; no AEGL-2 effects noted						
Rats repeatedly exposed to 40 ppm for 8 hours developed only moderate lung congestion (Shell Chemical Corp., 1957)	10	2	16	11	5.7	4.0
Consistent with the proposed AEGL-2 values but maybe the same study						

SUMMARY OF SUPPORTING/ALTERNATIVE AEGL-3 DERIVATIONS (ppm)						
Endpoint/Rationale/Reference	**UF**	***n***	**30 m**	**1 h**	**4 h**	**8 h**
NOEL for death in mice exposed to 500 ppm for 0.5 hours (Union Carbide, 1951)	10	2	50	35	18	13
Slightly higher than proposed AEGL-3 values						
Rats repeatedly exposed to 60 ppm for 7 hr: reversible irritation except persistent eye discharge; 1 death by end of study (Dunlap et al., 1958)	10	2	22	16	7.9	5.6
Chronic exposure: no deaths noted in acute studies at this level; unclear if eye dischrge the same as lacrimation						
1-hour LC_{01} of 93.1 ppm in mice estimated from Dunlap et al., 1958	10	2	13	9.3	4.7	3.3
	10	1	19	9.3	2.3	1.2
Calculated LC_{01} value of 93.1 ppm is well above the NOEL of 200 ppm in mice, rats, and rabbits						

Using the *n* derived from the LC_{50} studies (Dunlap et al., 1958), and playing conservative and rounding the number to 1, one obtains the following values:

SUMMARY/RELATIONSHIP OF AEGL VALUES (ppm) for *n* = 1				
Classification	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	1.8	1.8	1.8	1.8
AEGL-2 (40 ppm for 7 hr; UF = 10)	56	28	7	3.5
AEGL-3 (NOEL: 200 ppm for 1 hr; UF = 10)	40	20	5	2.5

SUMMARY/RELATIONSHIP OF AEGL VALUES (ppm) for *n* = 1				
Classification	**30-Minute**	**1-Hour**	**4-Hour**	**8-Hour**
AEGL-1	1.8	1.8	1.8	1.8
AEGL-2 (20 ppm for 7 hr; UF = 10)	28	14	3.5	1.8
AEGL-3 (NOEL: 200 ppm for 1 hr; UF = 10)	40	20	5	2.5

AEGL-1 (ppm)			
30 minutes	1 hour	4 hours	8 hours

AEGL-2 (ppm)			
30 minutes	1 hour	4 hours	8 hours

AEGL-3 (ppm)			
30 minutes	1 hour	4 hours	8 hours

National Advisory Committee (NAC)
for Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances
Final Meeting 6 Highlights
Green, 3rd Floor, Ariel Rios Building
1200 Pennsylvania Avenue, NW
Washington, D.C.
June 9-11, 1997

INTRODUCTION

George Rusch (NAC/AEGL Chair) opened the meeting and reflected on the fact this meeting represented the first anniversary of the convening of the NAC/AEGL. The highlights of the meeting are described below and the meeting agenda (Attachment 1) and attendee list (Attachment 2) are affixed. The NAC- 5 highlights were approved without changes (Appendix A).

Prior to discussion of AEGL priority chemicals, Roger Garrett (Program Director) addressed several issues of importance to NAC/AEGL functions: (1) standing operating procedures for the NAC/AEGL, (2) attendance at NAC/AEGL meetings, (3) status of NAC/AEGL products for the Federal Register and, (4) NAC/AEGL member responsibilities.

(1) Standing Operating Procedures (SOP) Workgroup for the NAC/AEGLs

Roger Garrett announced the formation of a workgroup to develop guidance procedures for the NAC/AEGL. He urged the SOP workgroup to start the planning and priorization immediately and have a progress report in the next meeting.

(2) Meeting Attendance

Roger stressed the importance of attendance at NAC/AEGL meetings as well as concern regarding arrival/departure inconsistencies. It is imperative to have full attendance throughout the duration of the meeting for optimum productivity and performance of the NAC/AEGL.

(3) Federal Register Submissions

Roger Garrett reviewed the process and progress pertaining to the AEGLs submitted to the Federal Register. Ten chemicals are currently ready for submission and it is expected that several more will be ready for submission following the deliberations of this meeting.

(4) NAC Member Responsibilities

Roger Garrett expressed concern that all NAC/AEGL members should be active as chemical managers and reviewers as well as providing input on draft TSDs to ORNL in a timely fashion, and coordinating document review during the NAC/AEGL meetings.

TECHNICAL DISCUSSIONS

Uncertainty Factor Workgroup Report (Richard Thomas)

The workgroup has had three teleconferences, the first being an organizational effort, the second noting background information on the various uncertainty factors used in the development of AEGLs, and the third addressing significant figure and rounding issues. The discussions on rounding and significant figures culminated in a motion to use two significant figures regardless of the relationship to the decimal point (Attachment 3).

Chemical-Specific Issues - Final Review of Proposed AEGLs

Arsine

Robert Young provided a brief overview of the AEGLs for arsine and a justification for recommending that AEGL-1 values for this chemical are not appropriate (Attachment 4). The justification was based upon the known steep dose-response for arsine and its mechanism of action (hemolysis) that may result in little margin between nontoxic exposures and lethal exposures, and the fact that toxicity may occur below the odor threshold. A motion to replace the AEGL-1 values of 0.1 ppm for arsine with "Not Appropriate" was unanimously approved (Appendix B).

Cyanogen chloride

Mark McClanahan affirmed that data for this chemical are limited and that commercial production can not be verified (the chemical appears to exist only as an intermediate in chemical processes). It was the consensus of the NAC [motion made by T. Hornshaw, seconded by R. Thomas: YES:27, NO:0] that the existing AEGL values be removed from the document and replaced with the narrative to the effect of "Information is inadequate for AEGL derivation. The NAC does not have commercial production data and, therefore, does not currently perceive the necessity to derive AEGLs" (Appendix C).

Hydrogen cyanide

Ernie Falke briefly reviewed pertinent information including the Wexler et al. 1947 report (Attachment 5). He stated that it is necessary to state if the dose used in this study was a bolus administration. The use of n=1 rather than n=2 for the ten Berge equation was also noted. An elaboration on justification of uncertainty factors is also needed. Three options were proposed regarding this document: (1) leave document as is, (2) re-evaluate the data, or (3) search for more data. George Rusch suggested that the document be revisited and that kinetic data be evaluated to provide insight into the route-to-route extrapolation issue.

Hydrogen fluoride

Sylvia Talmage summarized the issues (Attachment 6) pertaining to the AEGL derivation for this chemical: (1) inconsistencies in data usage, (2) inconsistencies in uncertainty factor application (i.e., 10 was used but 3 may be more appropriate), and (3) adjustment of the toxicity endpoint. Because some of the suggested changes were large and the NAC needed to refamiliarize themselves with the TSD, George Rusch recommended that this chemical be tabled until the next meeting whereupon relevant issues will be revisited.

Methyl mercaptan

Doan Hansen provided a brief overview (Attachment 7) of odor threshold, an important issue for this chemical. Following discussion regarding odor threshold and derivation of the AEGL-1 values, it was the consensus of the NAC to expand the rationale for the AEGL-1 values. The AEGL-2 and AEGL-3 values will remain unchanged.

AEGL PRIORITY CHEMICALS

Ammonia
CAS Reg. No. 7664-41-7

Chemical Manager: Larry Gephart , Exxon Biomedical
Staff Scientist: Kowetha Davidson, Oak Ridge National Laboratory

Larry Gephart provided an introduction and general update regarding the comments on proposed AEGLs from external reviews and interested parties (Attachment 8). Kowetha Davidson summarized the current status of the ammonia AEGLs, their respective data sets, and derivations (Attachment 9). Robert Michaels (Ram Trac Corp.) reiterated previous concerns regarding several issues (e.g., inconsistencies between proposed AEGL-3 values and actual lethality levels, assumption of n=2 in the ten Berge equation, mice as an appropriate model species, concerns regarding human equivalent concentrations, concerns regarding AEGL-2 values being reduced with exposure duration) (Attachment 10). Representatives for The Fertilizer Institute (TFI), Chris Leason and Barry Hooberman, provided comments on previous draft AEGL values (e.g., selection of endpoints) and comments regarding responsibilities of the NAC to respond to external comments on a previous draft of the ammonia technical support document (Attachment 11). Paul Tobin (Designated Federal Officer) responded that the legal responsibilities regarding mode and method of response are outside of the NACs' purview. Several NAC members noted that review of the Environ and Ram Trac reports simply represented alternate interpretations of data. Discussions focusing on specific AEGLs followed. AEGL-3 discussions focused on the use of an estimated lethality threshold as opposed to a NOAEL, and also the application of an uncertainty factor for individual variability (10 vs 3). It was the consensus of the NAC that the LC_{01} was appropriate for deriving the AEGL-3 and that a UF of 3 was justified for accounting for individual variability. The AEGL-3 values as shown in the summary table were appproved [motion made by E. Falke, seconded by R. Thomas: YES:23, NO:3, ABSTAIN:5]. The AEGL-2 discussions considered the relevance of the selected endpoint and its severity as applicable to AEGL-2. The NAC discussed the 1-hour exposure concentrations (110 or 140 ppm) associated with different levels of effects (baseline values) and the n-value (n = 2 or 4) for the $C^n \times t = k$ equation. The following table shows the baseline values and the resulting AEGL values extrapolated over the relevant time points (UF=1):

	AEGL values considered by the NAC				
Baseline values	5-min	30-min	1-hour	4-hours	8-hours
110 ppm; n=2	380 ppm	160 ppm	110 ppm	55 ppm	38 ppm
110 ppm; n=4	200 ppm	130 ppm	110 ppm	78 ppm	65 ppm
140 ppm; n=2	480 ppm	220 ppm	140 ppm	70 ppm	50 ppm
110 ppm; n=2 (60 -min)	380 ppm	160 ppm	110 ppm	110 ppm	110 ppm

It was also proposed that 110 ppm be used for all time points. It was the consensus of the NAC the AEGL-2 be based upon a 60-min exposure to 110 ppm resulting in unbearable eye irritation, odor, and nasopharyngeal irritation [motion made by S. Barbee, seconded by L. Koller: YES:18, NO:7, ABSTAIN:2]. The AEGL-2 values for 5 minutes and 30 minutes were based on ten Berge's equation where n=2, and the 1-, 4-, and 8-hour values were flatlined at 110 ppm (Appendix D).

SUMMARY OF PROPOSED AEGL VALUES FOR AMMONIA					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1 [a,b]	25 ppm 17 mg/m^3	25 ppm 17 mg/m^3	25 ppm 17 mg/m^3	25 ppm 17 mg/m^3	odor
AEGL-2 [b]	160 ppm 112 mg/m^3	110 ppm 77 mg/m^3	110 ppm 77 mg/m^3	110 ppm 77 mg/m^3	severe eye irritation, odor, nasopharyngeal irritation
AEGL-3 [b]	1600 ppm 1119 mg/m^3	1100 ppm 769 mg/m^3	550 ppm 385 mg/m^3	390 ppm 273 mg/m^3	LC_{01} in mice

[a] AEGL-1 values previously adopted by the Committee were not changed.
[b] Proposed 5-min AEGL-3 of 3800 ppm (2675 mg/m^3), 5-min AEGL-2 of 380 ppm (266 mg/m^3), and 5-min AEGL-1 of 25 ppm (17 mg/m^3) were also approved, respectively.

Toluene 2,4-& 2,6-diisocyanates
CAS Reg. Nos. 91-08-7 and 584-84-9

Chemical Manager: **Steve Barbee, Olin Corporation**
Chemical Reviewers: **Jonathan Borak, ACOEM**
Doan Hansen, Brookhaven National Laboratory
Staff Scientist: Carol Forsyth, Oak Ridge National Laboratory

Steve Barbee reviewed the AEGL values for TDI from the last NAC deliberation (Attachment 12). Discussions followed regarding endpoints for AEGL-2. The endpoint of reversible pulmonary inflammation (Duncan et al., 1962) was supported by human data (Henschler et al., 1962). For AEGL-1, discussions revolved around data showing changes in airway resistance (FEV_1) in asthmatics and other signs/symptoms (chest tightness, cough, dyspnea, headache) reported by Bauer (1985). The proposed AEGL-1 and AEGL-2 values shown in the table below were approved by the NAC [motion made by Z. Post, seconded by L. Koller: AEGL-1, YES:26, NO:2, ABSTAIN:1; motion made by Z. Post, seconded by L. Koller: AEGL-2 YES:28, NO:0, ABSTAIN:1] (Appendix E). For AEGL-1, it was noted that a statement be added to the technical support document indicating that the proposed values will not be protective for isocyanate-sensitized individuals. The proposed AEGL-3 values were approved at NAC Meeting No. 5.

SUMMARY OF PROPOSED AEGL VALUES FOR 2,4 AND 2,6 TDI					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1	0.02 ppm 0.14 mg/m^3	0.02 ppm 0.14 mg/m^3	0.01 ppm 0.07 mg/m^3	0.01 ppm 0.07 mg/m^3	FEV_1 changes and clinical signs
AEGL-2	0.2 ppm 1.42 mg/m^3	0.1 ppm 0.71 mg/m^3	0.06 ppm 0.43 mg/m^3	0.06 ppm 0.43 mg/m^3	pulmonary histopathologic changes
AEGL-3[a]	0.92 ppm 6.6 mg/m^3	0.65 ppm 4.6 mg/m^3	0.32 ppm 2.3 mg/m^3	0.23 ppm 1.6 mg/m^3	lethality threshold estimated from 4-hr LC_{50} for mice

[a] AEGL-3 values were approved at NAC Meeting No. 5, June 9-11, 1997.

Chlorine trifluoride
CAS Reg. No. 7790-91-2

Chemical Manager: **Kyle Blackman, FEMA**
Chemical Reviewers: **Robert Benson, U.S. EPA**
Nancy Kim, New York State Dept. of Health
Mark McClanahan, CDC
Staff Scientist: Sylvia Talmage, Oak Ridge National Laboratory

Kyle Blackman made brief introductory remarks about chlorine trifluoride (Attachment 13) followed by an overview by Sylvia Talmage of the derivation of AEGL values for this chemical (Attachment 14). Following discussion, the following values were approved by the NAC/AEGL: AEGL-1 [motion made by E. Falke, seconded by J. Hinz: YES:24, NO:4, ABSTAIN:1]; AEGL-2 [motion made by E. Falke, seconded by J. Hinz: YES:26, NO:2, ABSTAIN:1]; AEGL-3 [motion made by E. Falke, seconded by J. Hinz: YES:26, NO:2, ABSTAIN:1] (Appendix F).

SUMMARY OF PROPOSED AEGL VALUES FOR CHLORINE TRIFLUORIDE					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1	0.70 ppm 2.7 mg/m^3	0.35 ppm 1.3 mg/m^3	0.09 ppm 0.34 mg/m^3	0.04 ppm 0.15 mg/m^3	threshold for notable discomfort
AEGL-2	6.2 ppm 24 mg/m^3	3.1 ppm 12 mg/m^3	0.77 ppm 2.9 mg/m^3	0.39 ppm 1.5 mg/m^3	strong irritation - dog
AEGL-3	27 ppm 103 mg/m^3	14 ppm 53 mg/m^3	3.4 ppm 13 mg/m^3	1.7 ppm 6.5 mg/m^3	threshold for lethality (LC_{01}) - mouse

Ethylenimine
CAS Reg. No. 151-56-4

Chemical Manager: **Mark McClanahan, CDC**
Chemical Reviewers: **Loren Koller, OSU**
Richard W. Niemeier, NIOSH
Staff Scientist: Kowetha Davidson, Oak Ridge National Laboratory

Mark McClanahan presented introductory material and Kowetha Davidson presented an overview of AEGL derivations for ethylenimine (Attachment 15). Following discussions regarding the concentration measurement in the human data sets and how to address the carcinogenicity issues, Steve Barbee proposed AEGL-2 and AEGL-3 values based upon respiratory effects and lethality endpoints, respectively, with a total uncertainty factor application of 10 (3 for intraspecies variability and 3 for interspecies variability). The proposed AEGL values were approved by the NAC/AEGL: AEGL-1 [motion made by S. Barbee, seconded by M. McClanahan: YES:26, NO:1, ASBSTAIN:1]; AEGL-2 [motion made by S. Barbee, seconded by M. McClanahan: YES:23, NO:4, ABSTAIN:1]; AEGL-3 [motion made by S. Barbee, seconded by M. McClanahan: YES:24, NO:3, ABSTAIN:1]. The TSD for ethylenimine should note the carcinogenicity issue as well as the possibility of delayed effects at AEGL levels (Appendix G).

SUMMARY OF PROPOSED AEGL VALUES FOR ETHYLENIMINE					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1	NR	NR	NR	NR	
AEGL-2	9.8 ppm 5.5 mg/m^3	4.6 ppm 2.6 mg/m^3	1.0 ppm 0.56 mg/m^3	0.47 ppm 0.26 mg/m^3	respiratory difficulty - guinea pig
AEGL-3	18 ppm 10 mg/m^3	9.6 ppm 5.5 mg/m^3	2.8 ppm 1.6 mg/m^3	1.5 ppm 0.84 mg/m^3	lethality threshold - rat

NR: No recommendation

Diborane
CAS Reg. No. 19287-45-7

Chemical Manager: **Jim Holler, ATSDR**
Chemical Reviewers: **George Rogers, AAPCC**
Robert Benson, U.S. EPA
Staff Scientist: Claudia Troxel, Oak Ridge National Laboratory

Claudia Troxel presented an overview of the derivation of AEGLs for diborane (Attachment 16). Following a very brief discussion, a motion was made by D. Hansen and seconded by W. Bress to approve values for AEGL-2 and AEGL-3, and adopt a "Not Appropriate" status for AEGL-1 (no sensory irritation and AEGL-2 values are below the odor threshold). The motion carried and the following proposed values were approved: AEGL-1 [YES:26, NO:2, ABSTAIN:1]; AEGL-2 [YES:22, NO:6, ABSTAIN:1]; AEGL-3 [YES:27, NO:1, ABSTAIN:1] (Appendix H).

SUMMARY OF PROPOSED AEGL VALUES FOR DIBORANE					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1	NA	NA	NA	NA	
AEGL-2	2.0 ppm 2.2 mg/m^3	1.0 ppm 1.1 mg/m^3	0.25 ppm 0.28 mg/m^3	0.13 ppm 0.14 mg/m^3	multifocal and/or diffuse epithelial degeneration in terminal bronchi
AEGL-3	7.3 ppm 8.0 mg/m^3	3.7 ppm 4.1 mg/m^3	0.92 ppm 1.0 mg/m^3	0.46 ppm 0.51 mg/m^3	LC_{01} - mouse

NA: Not appropriate

Allylamine
CAS Reg. No. 107-11-9

Chemical Manager: **Loren Koller, OSU**
Chemical Reviewers: **Mark McClanahan, CDC**
Robert Hazen, New Jersey
Staff Scientist: Sylvia Milanez, Oak Ridge National Laboratory

Sylvia Milanez provided an overview of the derivation of proposed AEGLs for allylamine (Attachment 17). The AEGL-3 values based upon lethality in rats were accepted as originally proposed in the TSD [motion made by L. Gephart, seconded by Z. Post: YES:25, NO:0, ABSTAIN:1]. Loren Koller led discussions regarding the selection of the exposure concentrations, endpoints, and uncertainty factors with which to derive the AEGL-2 values for allylamine. Following discussions, four options were presented: (1) base all AEGL-2 values on the RD_{50}, (2) use an irritation threshold in human subjects for the 30-min and 1-hour values, and cardiotoxic effects in rats (40 ppm for 8 hours, UF=100) for the 4- and 8-hour values, (3) use an 8-hour exposure to 40 ppm (cardiotoxicity, UF=100), or (4) use the values as originally proposed in the draft TSD based upon decreased body weight gain in rats at 10 ppm, UF=30). A poll of the Committee appeared to favor the originally proposed values or those based upon the third option. The NAC/AEGL approved the AEGL-2 values based upon cardiotoxicity following an 8-hour exposure to 40 ppm [motion made by Z. Post, seconded by J. Hinz: YES:22, NO:2] (Appendix I). Because the odor threshold is at or above the 4- and 8-hour AEGL-2 values, it was the consensus [motion made by E. Falke, seconded by R. Thomas: YES:17, NO:7] of the NAC/AEGL that AEGL-1 values be considered inappropriate for allylamine (Appendix I). The AEGLs for allylamine are summarized in the following table.

SUMMARY OF PROPOSED AEGL VALUES FOR ALLYLAMINE					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1	NA	NA	NA	NA	
AEGL-2	11 ppm 25 mg/m^3	4.7 ppm 11 mg/m^3	0.91 ppm 2.1 mg/m^3	0.40 ppm 0.93 mg/m^3	cardiotoxicity following 8-hr exposure to 40 ppm
AEGL-3	40 ppm 94 mg/m^3	18 ppm 42 mg/m^3	3.5 ppm 8.1 mg/m^3	2.3 ppm 5.4 mg/m^3	lethality (LC_{01}) in rats exposed for 1, 4, or 8 hrs

NA: Not appropriate

Hydrogen chloride
CAS Reg. No. 7647-01-6

Chemical Manager: **John Hinz, USAF**
Chemical Reviewers: **Larry Gephart, Exxon Biomedical**
Nancy Kim, New York State Health Department
Staff Scientist: Cheryl Bast, Oak Ridge National Laboratory

An overview of hydrogen chloride issues from the perspective of the U.S. Air Force Rocket Emissions Workgroup was provided by John Hinz (Attachment 18). It was emphasized that HCl exposure is a pertinent issue relative to rocket launches (ground cloud exposures to mission-critical personnel, on-base personnel

distant to the launch site, and civilian off-base population), and that such exposure potential occurs with regularity as opposed to the single accident scenarios normally assumed for AEGL application. Cheryl Bast reviewed the limited data available for derivation of AEGLs as well as the derivation of the AEGLs proposed in the draft TSD (Attachment 19). Following discussion, it was unanimously agreed that the AEGL-1 be set at 1.8 ppm for all time points [motion made by D. Hansen, seconded by S. Barbee: YES:25, NO:0]. For AEGL-2, discussions focused on incidences of histopathologic findings in the rats from the Stavert et al. (1991) study and that the proposed 1-hour AEGL-2 was higher than the ERPG and SPEGL. Following discussions regarding uncertainty factor applications, AEGL-2 values were approved by the Committee [motion made by W. Bress, seconded by R. Benson: YES:23, NO:1]. AEGL-3 values were accepted as originally presented in the TSD [motion made by L. Koller, seconded by D. Hansen: YES:16, NO:5]. The values for HCl are shown in the following table. (Appendix J)

SUMMARY OF PROPOSED AEGL VALUES FOR HYDROGEN CHLORIDE					
Classification	30-min	1-hour	4-hour	8-hour	Endpoint
AEGL-1	1.8 ppm 2.7 mg/m^3	1.8 ppm 2.7 mg/m^3	1.8 ppm 2.7 mg/m^3	1.8 ppm 2.7 mg/m^3	no effect level in humans (exercising asthmatics)
AEGL-2	43 ppm 64 mg/m^3	22 ppm 33 mg/m^3	5.4 ppm 8.0 mg/m^3	2.7 ppm 4.0 mg/m^3	histopathology in rats
AEGL-3	210 ppm 313 mg/m^3	104 ppm 155 mg/m^3	26 ppm 39 mg/m^3	13 ppm 19 mg/m^3	1-hr rat LC_{50}

ADMINISTRATIVE ISSUES

Meeting Commencement and Adjournment

It was the consensus of the NAC/AEGL that the meeting will continue to start at 10:00 a.m. the first day but that commencement will be 8:00 a.m. for days 2 and 3. Adjournment on day 3 will be at 12:30 p.m.

General Comments

In an open comment session, George Rusch requested comments from the committee. These included but were not limited to:

- a need for clear presentation of how AEGL values are derived
- a need for carefully developed standard operating procedures that allow for time- and cost-effective document preparation and approval of values
- need for a cover memo on document revisions to note major changes and a date on each draft
- a need to identify research needs where appropriate
- improvement in the meeting facility audio equipment and in visual aids used by presenters
- necessity of focusing on science vs policy procedures
- availability of a table/chart of NAC areas-of-expertise
- NAC should avoid dogmatic views and excessive focus on methodologies rather than human health issues
- the formation of separate groups for chemical-specific evaluations
- availability of chemical-specific experts as *ad hoc* participants at NAC/AEGL meetings
- a need to focus on cancer assessments for acute exposures

- Paul Tobin emphasized that the copies of TSDs in the foyer of the meeting room are for visitors/observers and NOT for NAC/AEGL members. Members are to bring their own copies to the

meeting

- For the standing operating procedures, some attention should be given to endpoints for AEGLs, application and interpretation of dispersion models and dose reconstruction, carcinogenicity and reproductive toxicity issues, disposition of Federal Register comments, and recourse if data are inadequate for AEGL derivation

Standing Operating Procedures (SOP) Workgroup

A workgroup to assist in the development of AEGL technical support document (TDS) was announced by Roger Garrett. The Standing Operating Procedures (SOP) Workgroup, chaired by Ernest Falke (U.S. EPA), will consist of George Alexeeff (CALEPA), Steven Barbee (Olin Corp.), David Belluck (MN Pollution Control), George Rogers (AAPCC), Kenneth Steel (DoD), and Robert Young (ORNL). George Rusch and Roger Garrett will serve as advisors. Based on an open discussion with the NAC/AEGL members, chaired by George Rusch on Tuesday, June 10, 1997, regarding the focus of the workgroup, a list of important areas releated to the development of AEGL values was compiled. This list has been orgnized into three major categories that are to be addressed initially by the workgroup. These include: (1) development of information and data for TSDs, (2) calculation of AEGL values, and (3) format and content of TSDs (Attachment 20). A 30-minute organizational meeting of the workgroup was held on Wednesday, June 11, prior to the regular NAC/AEGL priority chemical review session. An effort will be made to focus on item No. 3 and to identify specific areas in item No. 2 that may be more easily addressed. Areas that were not considered to be of immediate concern to the workgroup were justification for chemical selection, review of AEGLs, membership, chemical manager roles, and identification of studies to fill data gaps.

Action Item: members of the SOP Workgroup will provide comments/thoughts on initial issues to Ernest Falke by June 28.

Future Meeting Dates

The following meeting dates were tentatively scheduled:
Meeting No. 7 - September 23-25, 1997
Meeting No. 8 - December 8-10, 1997

The date and location of the March and June 1998 meetings were briefly discussed but no decisions made.

The meeting highlights were prepared by Robert Young and Po-Yung Lu, ORNL.

Areas to be Addressed by SOP Workgroup

1. Development of Information and Data for TSDs.
   a. Possible approaches to supplements to literature/data searches
   b. Guidelines/criteria for quality ranking of papers/data and confidence in studies
   c. Possible use or graphs to evaluate/utilize data
   d. Archives - who, how long, where

2. Calculations of AEGL Values
   a. Refinement of AEGL-1 definition (possibly AEGL-2 also)
   b. Endpoints for selection of AEGL levels (and their significance, including significance of odor & behavioral criteria)
   c. Dose extrapolation techniques
   d. Guidelines/criteria for use of NOAELs and LOAELs
   e. Guidelines/criteria for uncertainty factors
   f. Guidelines/criteria for modifying factors
   g. Guidelines/criteria for time scaling (algorithm and short to long term scaling)
   h. Guidelines/criteria for exposure data, exposure assumptions, and exposure models
   I. Guidelines/criteria for scientific rationale
   j. Policy for known and suspect carcinogens
   k. Scientific basis for decision
   l. Endpoints - key ones - priority
   m. What constitutes insufficient information
   n. Fetotoxicity, Ca risk

3. Format and Content of TSDs
   a. Format for summary table
   b. Consistency of data tables
   c. Potential inclusion of special data/info (e.g., chemical structure, relevant P/C properties, uses, etc.)
   d. Guidelines/criteria for presentation of scientific rationale
   e. Guidelines/criteria for describing/presenting calculations
   f. Potential inclusion of graphic descriptions of data
   g. Format/consistency in developing revised TSDs
   h. Guidelines/criteria for consistent description of data

LIST OF ATTACHMENTS

The attachments were distributed during the meeting and will be filed in the EPA Docket Office.

1. NAC /AEGL Meeting No. 6 Agenda
2. NAC/AEGL Meeting No. 6 Attendee List
3. Consensus of Operating Procedures - Richard Thomas
4. Data analysis of Arsine - Bob Young
5. Data analysis of Hydrogen cyanide - Ernie Falke
6. Data analysis of Hydrogen fluoride - Sylvia Talmage
7. Data analysis of Methylmercaptan - Doan Hansen
8. Ammonia AEGL Update - Larry Gephart
9. Data analysis of Ammonia -Kowetha Davidson
10. Public comment from RAM TRAC - Robert Michaels
11. Public comment from ENVIRON - Chris Leason and Barry Hooberman
12. Threshold for Sensitization - Steve Barbee
13. ClF3 hydrolysis products - Kyle Blackman
14. Data analysis of ClF3 - Sylvia Talamge
15. Data analysis of Ethylenimine - Kowetha Davidson
16. Data analysis of Diborane - Claudia Troxel
17. Data analysis of Allylamine - Sylvia Milanez
18. HCl: An Air Force-based Perspective - John Hinz
19. Data analysis of HCl - Cheryl Bast
20. SOP Workgroup Report

LIST OF APPENDICES

A. Approved NAC/AEGL- 5 Meeting Highlights
B. Ballot for Arsine
C. Ballot for Cyanogen chloride
D. Ballot for Ammonia
E. Ballot for TDI
F. Ballot for ClF3
G. Ballot for Ethelenimine
H. Ballot for Diborane
I. Ballot for Allylamine
J. Ballot for Hydrogen chloride

Date of AEGL NAC meeting: 9/23/97 **Chemical:** HYDROGEN FLUORIDE (REVISED VALUES)

NAC Member	AEGL1	AEGL2 10Min/60	AEGL3
George Alexeeff		Y	
Steven Barbee		Y	
Lynn Beasley		Y	
David Belluck		Y	
Robert Benson		Y	
Kyle Blackman		Y	
Jonathan Borak		A	
William Bress		Y	
Luz Claudio		Y	
Guy Colonna		A	
George Cushmac		Y	
Marion F. Ehrich		A	
Ernest Falke		Y	
Larry Gephart		Y	
John Hinz		Y	
Jim Holler		Y	
Thomas C. Hornshaw		Y	

NAC Member	AEGL1	AEGL2	AEGL3
Nancy K. Kim		Y	
Loren Koller		Y	
Glenn Leach		A	
Mark A. McClanahan		Y	
John S. Morawetz		A	
Richard W. Niemeier		Y	
Willia Pepelko		Y	
Zarena Post		Y	
George Rodgers		Y	
George Rusch, Chair		P	
Bob Snyder		Y	
Thomas J. Sobotka		Y	
Kenneth Still		Y	
Patricia Ann Talcott		A	
Richard Thomas		A	
Thomas Tuccinardi/ Doan Hansen		A A	
TALLY			

P=PASS A=ABSENT

10 MIN / 30 MIN

PPM, (mg/m³)	30 Min	60 Min	H	8Hr
AEGL 1	,( )	,( )	,)	,( )
AEGL 2	95ppm ,(ppm	24 ,( )	12 ,)	8.6 ,( )
AEGL 3	,( )	,( )	,)	,( )

AEGL 1 Motion: _____ **Second:** _____

AEGL 2 Motion: E. Falke **Second:** K. Blackman 10 MIN
~~E. Falke~~ ~~R. Niemeier~~ 30 MIN / 1 HR
Z. Post H. KIM

AEGL 3 Motion: _____ **Second:** _____

Approved by Chair: _____ **DFO:** _____ **Date:** _____

Comments: WILLIAM HAZEN (N.J.) INTENDS TO RESIGN FROM THE COMMITTEE (NOT LISTED ABOVE)

Date of AEGL NAC meeting: 9/23/97 **Chemical:** HYDROGEN FLUORIDE (REVISED VALUES)

NAC Member	AEGL1	AEGL2 (10 min)	AEGL2 (30 min)	AEGL3
George Alexeeff		Y	N	
Steven Barbee		Y	Y	
Lynn Beasley		Y	Y	
David Belluck		Y	Y	
Robert Benson		Y	Y	
Kyle Blackman		Y	Y	
Jonathan Borak		A	A	
William Bress		Y	Y	
Luz Claudio		Y	Y	
Guy Colonna		A	A	
George Cushmac		Y	Y	
Marion F. Ehrich		A	A	
Ernest Falke		Y	Y	
Larry Gephart		Y	P	
John Hinz		Y	Y	
Jim Holler		Y	Y	
Thomas C. Hornshaw		Y	Y	

NAC Member	AEGL1	AEGL2 (10 min)	AEGL2 (30 min)	AEGL3
Nancy K. Kim		Y	Y	
Loren Koller		Y	Y	
Glenn Leach		A	A	
Mark A. McClanahan		Y	Y	
John S. Morawetz		A	A	
Richard W. Niemeier		Y	Y	
Willia Pepelko		Y	Y	
Zarena Post		Y	Y	
George Rodgers		Y	Y	
George Rusch, Chair		P	P	
Bob Snyder		Y	Y	
Thomas J. Sobotka		Y	Y	
Kenneth Still		Y	Y	
Patricia Ann Talcott		A	A	
Richard Thomas		A	A	
Thomas Tuccinardi/ Doan Hansen		A A	A A	
TALLY		24/24	23/24	

P = PASS A = ABSENT

PPM. (mg/m^3)		10 min 30 Min	60 Min	4 Hr	8Hr
AEGL 1		,( )	,( )	,( )	,( )
AEGL 2	95	34 ,( )	24 ,( )	12 ,( )	8.6 ,( )
AEGL 3		,( )	,( )	,( )	,( )

AEGL 1 Motion: E. FALKE **Second:** K. BLACKMAN 10 MIN

AEGL 2 Motion: Z. POST **Second:** N. KIM 30 MIN / 1 HR

AEGL 3 Motion: W. BRESS **Second:** R. BENSON Use original AEGL-3 Values. — UNANIMOUS

Approved by Chair: [signature] **DFO:** [signature] **Date:** 9/23/97

Comments: WILLIAM HAZEN (NJ) RESIGNED

Date of AEGL NAC meeting: 9/23/97 **Chemical:** DIMETHYL DICHLOROSILANE

NAC Member	AEGL1	AEGL2	AEGL3	NAC Member	AEGL1	AEGL2	AEGL3
George Alexeeff	Y	Y		Nancy K. Kim	P	P	
Steven Barbee	Y	Y		Loren Koller	Y	Y	
Lynn Beasley	Y	Y		Glenn Leach	A	A	
David Belluck	Y	Y		Mark A. McClanahan	Y	Y	
Robert Benson	P	P		John S. Morawetz	A	A	
Kyle Blackman	Y	Y		Richard W. Niemeier	Y	Y	
Jonathan Borak	A	A		Willia Pepelko	A	A	
William Bress	Y	Y		Zarena Post	Y	Y	
Luz Claudio	~~A~~ P	P		George Rodgers	Y	Y	
Guy Colonna	A	A		George Rusch, Chair	Y	Y	
George Cushmac	Y	Y		Bob Snyder	Y	Y	
Marion F. Ehrich	A	A		Thomas J. Sobotka	Y	Y	
Ernest Falke	Y	Y		Kenneth Still	Y	Y	
Larry Gephart	Y	Y		Patricia Ann Talcott	A	A	
John Hinz	Y	Y		Richard Thomas	A	A	
Jim Holler	Y	Y		Thomas Tuccinardi/ Doan Hansen			
Thomas C. Hornshaw	Y	Y					
				TALLY	21/21	21/21	

PPM, (mg/m³)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	0.45 ,( )	0.45 ,( )	0.45 ,( )	0.45 ,( )
AEGL 2	11 ,( )	5.5 ,( )	1.4 ,( )	0.68 ,( )
AEGL 3	,( )	,( )	,( )	,( )

AEGL 1 Motion: G Rogers **Second:** Bill Bress

AEGL 2 Motion: G Rogers ~~B. Bress~~ **Second:** Bill Bress

AEGL 3 Motion: NOT UP FOR REVISION **Second:** _____

Approved by Chair: _____ **DFO:** _____ **Date:** 9/23/97

Comments:

Date of AEGL NAC meeting: 9/24/97 **Chemical:** METHYL CHLOROFORMATE

NAC Member	AEGL1	AEGL2	AEGL3
George Alexeeff		P	P
Steven Barbee		Y	Y
Lynn Beasley		Y	Y
David Belluck		~~P~~ N	~~P~~ N
Robert Benson		Y	Y
Kyle Blackman		N	N
Jonathan Borak		A	A
William Bress		Y	Y
Luz Claudio		Y	Y
Guy Colonna		A	A
George Cushmac		Y	Y
Marion F. Ehrich		N	N
Ernest Falke		Y	Y
Larry Gephart		N	N
John Hinz		N	N
Jim Holler		Y	Y
Thomas C. Hornshaw		N	N

NAC Member	AEGL1	AEGL2	AEGL3
Nancy K. Kim		P	P
Loren Koller		Y	Y
Glenn Leach		A	A
Mark A. McClanahan		Y	Y
John S. Morawetz		A	A
Richard W. Niemeier		Y	Y
Willia Pepelko		N	N
Zarena Post		Y	Y
George Rodgers		Y	Y
George Rusch, Chair		Y	Y
Bob Snyder		N	N
Thomas J. Sobotka		A	A
Kenneth Still		Y	Y
Patricia Ann Talcott		A	A
Richard Thomas		A	A
Thomas Tuccinardi/ Doan Hansen		A A	A A
TALLY		15/22 ~~17~~ 15/23 2P	

P = PASS (ABSTAIN)

PPM, (mg/m³)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	,( )	,( )	,( )	,( )
AEGL 2	0.36 ,(1.4)	0.24 ,( )	0.13 ,(0.51)	0.09 ,(0.35)
AEGL 3	1.2 ,(4.7)	0.87 ,( )	0.43 ,(1.7)	0.31 ,(1.2)

AEGL 1 Motion: _____ **Second:** _____

AEGL 2 Motion: Koller **Second:** Hinz

AEGL 3 Motion: Koller **Second:** Hinz

Approved by Chair: [signature] **DFO:** [signature] **Date:** 9/24/97

Comments:

Date of AEGL NAC meeting: 9/24/97 **Chemical:** PROPYLENE OXIDE

NAC Member	AEGL1	AEGL2	AEGL3	NAC Member	AEGL1	AEGL2	AEGL3
George Alexeeff	Y	Ab	Y	Nancy K. Kim	Y	Y	Y
Steven Barbee	A	A	A	Loren Koller	Y	Y	N
Lynn Beasley	A	A	Y	Glenn Leach	A	A	A
David Belluck	Y	Ab	Y	Mark A. McClanahan	Y	Y	N
Robert Benson	Y	Y	Y	John S. Morawetz	A	A	A
Kyle Blackman	Y	Y	Y	Richard W. Niemeier	Y	Y	Ab
Jonathan Borak	A	A	A	Willia Pepelko	A	A	A
William Bress	Y	Ab	Y	Zarena Post	Y	Y	Y
Luz Claudio	Y	Y	Y	George Rodgers	Y	Y	Y
Guy Colonna	A	A	A	George Rusch, Chair	Y	Y	Y
George Cushmac	Y	Y	Y	Bob Snyder	Y	Y	Y
Marion F. Ehrich	A	A	Y	Thomas J. Sobotka	A	A	A
Ernest Falke	Ab	Y	Y	Kenneth Still	Y	Y	Y
Larry Gephart	Y	Y	N	Patricia Ann Talcott	A	A	A
John Hinz	Y	Ab	Ab	Richard Thomas	A	A	A
Jim Holler	Y	Y	Y	Thomas Tuccinardi/ Doan Hansen	A A	A A	A A
Thomas C. Hornshaw	Y	Y	N				
				TALLY	20/20	17/17	17/21
					Ab=1	Ab=4	Ab=2

Ab = ABSTAIN
A = ABSENT

PPM, (mg/m³)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	NA ,( )	NA ,( )	NA ,( )	NA ,( )
AEGL 2	260 ,( )	140 ,( )	39 ,( )	21 ,( )
AEGL 3	570 ,( )	300 ,( )	86 ,( )	46 ,( )

NA = NOT APPLICABLE (INSUFFICIENT DATA)
A = ABSENT

AEGL 1 Motion: M. McClanahan **Second:** D. Belluck

AEGL 2 Motion: M. McClanahan **Second:** L. Koller

AEGL 3 Motion: J. Hinz **Second:** W. Bress

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 9/24/97

Comments:

Date of AEGL NAC meeting: 9/25/97 **Chemical:** ACRYLYL CHLORIDE *

NAC Member	AEGL1	AEGL2	AEGL3	NAC Member	AEGL1	AEGL2	AEGL3
George Alexeeff				Nancy K. Kim			
Steven Barbee				Loren Koller			
Lynn Beasley				Glenn Leach			
David Belluck				Mark A. McClanahan			
Robert Benson				John S. Morawetz			
Kyle Blackman				Richard W. Niemeier			
Jonathan Borak				Willia Pepelko			
William Bress				Zarena Post			
Luz Claudio				George Rodgers			
Guy Colonna				George Rusch, Chair			
George Cushmac				Bob Snyder			
Marion F. Ehrich				Thomas J. Sobotka			
Ernest Falke				Kenneth Still			
Larry Gephart				Patricia Ann Talcott			
John Hinz				Richard Thomas			
Jim Holler				Thomas Tuccinardi/ Doan Hansen			
Thomas C. Hornshaw							
				TALLY			

* PROPOSAL TO SEEK MORE DATA TO SUPPORT DEVELOPMENT OF AEGL VALUES - UNANIMOUS

PPM, (mg/m³)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	,( )	,( )	,( )	,( )
AEGL 2	,( )	,( )	,( )	,( )
AEGL 3	,( )	,( )	,( )	,( )

AEGL 1 Motion: _____ **Second:** Kyle Blackman

AEGL 2 Motion: Loren Koller **Second:** _____

AEGL 3 Motion: _____ **Second:** _____

Approved by Chair: _____ **DFO:** _____ **Date:** 9/25/97

Comments:

Date of AEGL NAC meeting: 9/25/97 **Chemical:** BORON TRICHLORIDE

NAC Member	AEGL1	AEGL2	AEGL3	NAC Member	AEGL1	AEGL2	AEGL3
George Alexeeff	Y	Y	Y	Nancy K. Kim	Y	Y	Y
Steven Barbee	A	A	A	Loren Koller	Y	Y	Y
Lynn Beasley	Y	Y	Y	Glenn Leach	A	A	A
David Belluck	Y	Y	Y	Mark A. McClanahan	Y	Y	Y
Robert Benson	Y	Y	Y	John S. Morawetz	A	A	A
Kyle Blackman	Y	Y	Y	Richard W. Niemeier	Y	Y	Y
Jonathan Borak	A	A	A	Willia Pepelko	Y	Y	Y
William Bress	Y	Y	Y	Zarena Post	Y	Y	Y
Luz Claudio	A	A	Y	George Rodgers	Y	Y	Y
Guy Colonna	A	A	A	George Rusch, Chair	Y	Y	Y
George Cushmac	Y	Y	Y	Bob Snyder	Y	Y	Y
Marion F. Ehrich	A	A	A	Thomas J. Sobotka	Y	Y	Y
Ernest Falke	Y	Y	Y	Kenneth Still	Y	Y	Y
Larry Gephart	Y	Y	Y	Patricia Ann Talcott	A	A	A
John Hinz	Y	Y	Y	Richard Thomas	A	A	A
Jim Holler	Y	Y	Y	Thomas Tuccinardi/ Doan Hansen	A A	A A	A A
Thomas C. Hornshaw	Y	Y	Y				
				TALLY			24/24

A = ABSENT

PPM, (mg/m³)	30 Min	60 Min	H	8Hr
AEGL 1 *	1.8 ,( )	1.8 ,( )	1.8 ,)	1.8 ,( )
AEGL 2 *	14 ,( )	7.3 ,( )	1.8 ,)	0.9 ,( )
AEGL 3	57 ,( )	28 ,( )	~~7.2~~ ! ,)	~~3.5~~ 3.5 ,( )

* 1/3 VALUE OF HCl used as guidance level.

AEGL 1 Motion: _____ **Second:** _____

AEGL 2 Motion: R. Snyder **Second:** N Kim

AEGL 3 Motion: George Rodgers **Second:** Tom Sobotka

Approved by Chair: George H. Rusch **DFO:** Paul S. Tobin **Date:** 9/25/97

Comments:

Date of AEGL NAC meeting: 9/25/97 **Chemical:** ALLYL ALCOHOL

NAC Member	AEGL1	AEGL2	AEGL3	NAC Member	AEGL1	AEGL2	AEGL3
George Alexeeff	A	A	A	Nancy K. Kim	Y	Y	Y
Steven Barbee	A	A	A	Loren Koller	Y	Y	Y
Lynn Beasley	Y	Y	Y	Glenn Leach	A	A	A
David Belluck	Y	N	Y	Mark A. McClanahan	Y	Y	Y
Robert Benson	N	N	Y	John S. Morawetz	A	A	A
Kyle Blackman	N	N	N	Richard W. Niemeier	Y	Y	Y
Jonathan Borak	A	A	A	Willia Pepelko	N	Y	Y
William Bress	Y	Y	Y	Zarena Post	Y	Y	Y
Luz Claudio	Y	N	Y	George Rodgers	A	A	A
Guy Colonna	A	A	A	George Rusch, Chair	Y	Y	Y
George Cushmac	Y	Y	Y	Bob Snyder	Y	Y	Y
Marion F. Ehrich	A	A	A	Thomas J. Sobotka	N	Y	Y
Ernest Falke	Y	Y	Y	Kenneth Still	Y	Y	Y
Larry Gephart	Y	Y	Y	Patricia Ann Talcott	A	A	A
John Hinz	Y	Y	Y	Richard Thomas	A	A	A
Jim Holler	Y	Y	Y	Thomas Tuccinardi/ Doan Hansen	A A	A A	A A
Thomas C. Hornshaw	Y	Y	Y				
				TALLY	18/22	18/22	21/22

PPM, (mg/m³)	30 Min	60 Min	4 Hr	8Hr
AEGL 1	1.8 ,( )	1.8 ,( )	1.8 ,( )	1.8 ,( )
AEGL 2	15 ,( )	11 ,( )	5.3 ,( )	3.7 ,( )
AEGL 3	35 ,( )	25 ,( )	13 ,( )	8.8 ,( )

AEGL 1 Motion: W. Bress **Second:** Z. Post

AEGL 2 Motion: R. Snyder **Second:** L. Koller

AEGL 3 Motion: J Hinz **Second:** W. Pepelko

Approved by Chair: [signature] **DFO:** Paul S. Tobin **Date:** 9/25/97

Comments: